# 1. INTRODUCTION

Alcohol related liver disease is the commonest liver disease in India[1]. At least 1 in 5 Indians is living with some kind of liver problem related to alcohol. Its incidence in India is on the raising trend[2].It also remains a major etiological factor for cirrhosis worldwide. WHO estimates 140 million people worldwide suffer from alcohol dependency causing damage to lives and economics[3].

Esophageal varices remain a serious complication in patients with alcoholic cirrhosis. Variceal bleeding is the second most common cause of mortality in patients with cirrhosis[4]. Development of esophageal varices in cirrhotics is 5-8% per year with 1 – 2% risk of bleeding. 30% of the patients bleed at the first time of diagnosis. Rupture of esophageal varices accounts for 10 – 30% of all cases of Upper Gastro Intestinal bleed with high mortality rate of 20%[5].

Currently as per recommendations all cirrhotic patients are advised to undergo screening by endoscopy at the time of diagnosis to identify those at high risk of bleeding varices and likely benefiting from primary prophylaxis. The above approach however imposes a significant burden on the endoscopy

units and also decreases patients compliance due to repeated testing. Moreover, in peripheral health centres endoscopy is not readily feasible[6,7].

Child Turcotte Pugh (CTP) score is a simple non invasive tool originally designed to assess the mortality in patients undergoing liver transplantation. It is now widely used in assessing the prognosis of patients with chronic liver disease (CLD). This non invasive tool can also be used to predict the occurrence and severity of esophageal varices on first encounter of the patients with alcoholic liver disease[8].

So in a tertiary referral centre like our institute – Madras Medical College, Chennai, with high patient inflow, these simple non endoscopic parameters based on the study will be useful to predict the incidence and severity of esophageal varices in patients with alcoholic liver disease. These parameters may also help the physicians practicing in rural areas where invasive endoscopic facilities are not readily feasible to initiate appropriate primary prophylaxis and further evaluation[5].

# 2. AIM & OBJECTIVES

The study on "**A STUDY ON CHILD PUGH SCORE AS A NON ENDOSCOPIC PREDICTOR OF OESOPHAGEAL VARICES IN PATIENTS WITH ALCOHOLIC LIVER DISEASE**" was carried out with the following objectives.

- To study the age and sex incidence of esophageal varices in patients with alcoholic liver disease
- To correlate Child Pugh Score with Oesophageal varices in patients with alcoholic liver cirrhosis.
- To use the Child Pugh score value as a predictor for oesophageal varices and to calculate its value in assessing the varices severity.
- To assess the significance of other non endoscopic variables for the presence of oesophageal varices.

# 3. REVIEW OF LITERATURE

## ALCOHOLISM:

## *LITERATURE:*

- ALD represent the oldest form of liver injury known ever to mankind.Evidence suggests that fermented beverages existed at least as early as the Neolithic period (cir. 10,000 BC) [9].
- Mr. Charles Lieber with his colleagues in 1975 published a groundbreaking research article in liver research, stating that alcohol per se is the prime factor for the greater prevalence of liver disease in alcoholic patients rather than dietary factors and malnutrition as thought earlier. This has led to the several decades of study on the harmful effects of alcohol and its liver metabolism.
- Alcohol remains a major cause of liver disease worldwide[1].
- It is the WORLDS THIRD largest factor for the disease burden.
- The harmful use of alcohol results in 2.5 million deaths each year most of the mortality being secondary to cirrhosis[10].Its incidence in

India is on the increasing trend. Almost 1 in 5 Indians suffer from liver problems related to alcohol.

## RISK FACTORS FOR ALCOHOLIC LIVER DISEASE

- **1. Quantity** and 2. **Duration of alcohol intake**are the prime risk factors involved in the development of alcoholic liver disease[10]. The relationship between the amounts of alcohol consumption with the development of liver disease was not clearly linear.

**Figure 1: Risk factor and association of Alcoholic Liver Disease[10]**

| Risk Factor | Comment |
|---|---|
| Quantity | In men, 40–80 g/d of ethanol produces fatty liver; 160 g/d for 10–20 years causes hepatitis or cirrhosis. Only 15% of alcoholics develop alcoholic liver disease. |
| Gender | Women exhibit increased susceptibility to alcoholic liver disease at amounts >20 g/d; two drinks per day is probably safe. |
| Hepatitis C | HCV infection concurrent with alcoholic liver disease is associated with younger age for severity, more advanced histology, and decreased survival. |
| Genetics | Patatin-like phospholipase domain-containing protein 3 (PNPLA3) has been associated with alcoholic cirrhosis. |
| Fatty liver | Alcohol injury does not require malnutrition, but obesity and nonalcoholic fatty liver are risk factors. Patients should receive vigorous attention to nutritional support. |

- The risk to cirrhosis increases with the intake of >60–80g/day of alcohol in males and >20g/day in females for more than 10 years[11, 12]. Though the development of cirrhosis is seen in only 6-41% of the individuals[11, 13].
- On estimating the alcohol consumption it was found that four ounce of wine, one beeror one ounce of 80% spirits all have same amount of alcohol(12 g)[10].
- The threshold to develop alcoholic liver disease was found to be higher in males, while females develops similar degrees of injury to the liver by taking significantly less quantity.This sex difference is the result from poorly understood body fat proportion, estrogen and effect of menstrual cycle and the metabolism of alcohol in the stomach due to varied gastric levels of alcohol dehydrogenase enzyme. One another factor identified is to the pattern of drinking. Drinking outside of meal times increases the risk of ALD by 2.7-fold[14]. Some researches define binge drinking as four drinks for females and five drinks for males in one sitting also shown to increase the risk of Alcoholic liver disease[15,16].

# METABOLISM OF ALCOHOL

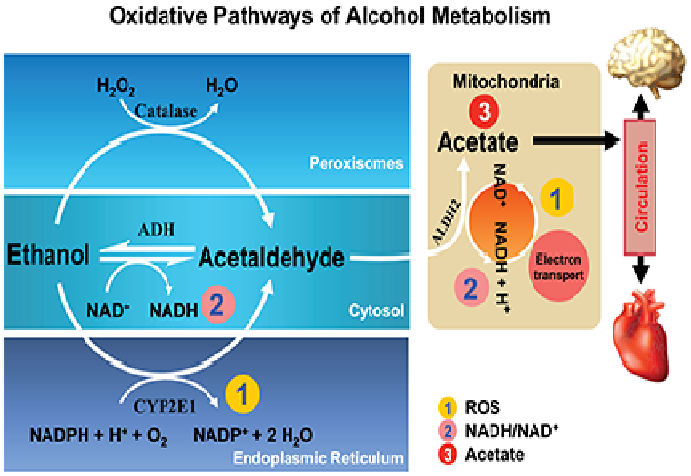
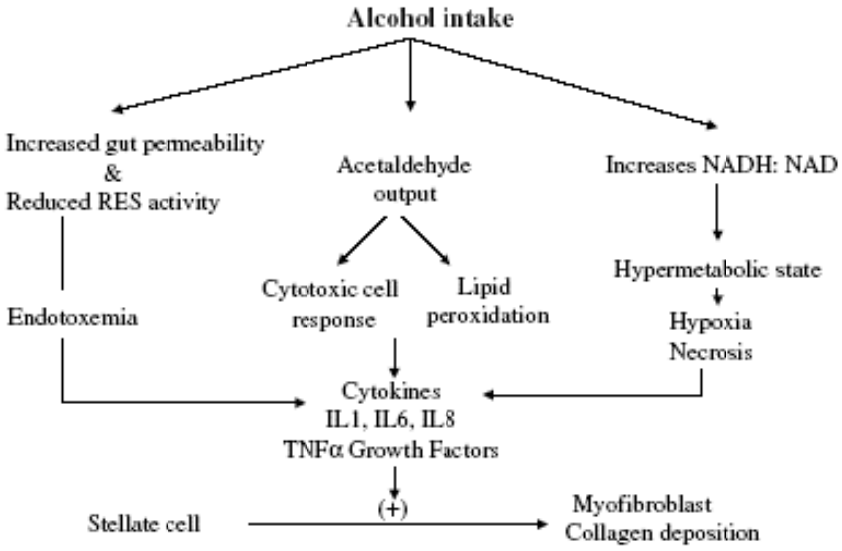



**Figure 2: ALCOHOL METABOLISM**

**Figure 3: PATHOGENESIS OF ALCOHOL IN ALD**

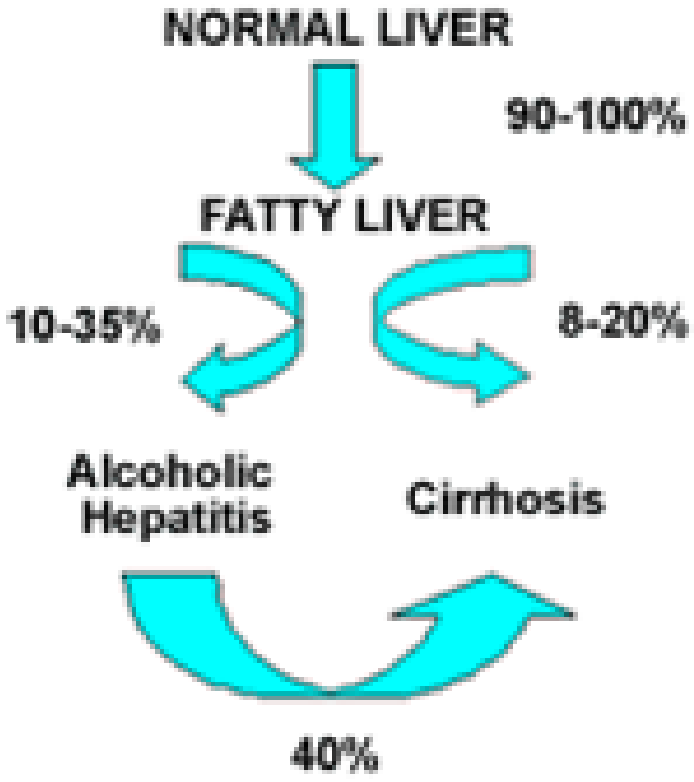


Alcoholic liver disease is the term used to describe the spectrum of the disease related to acute and chronic alcoholism.

The sequential changes are described in the following headings:

- FATTY LIVER( ALCOHOLIC STEATOSIS)
- ALCOHOLIC HEPATITIS
- ALCOHOLIC CIRRHOSIS

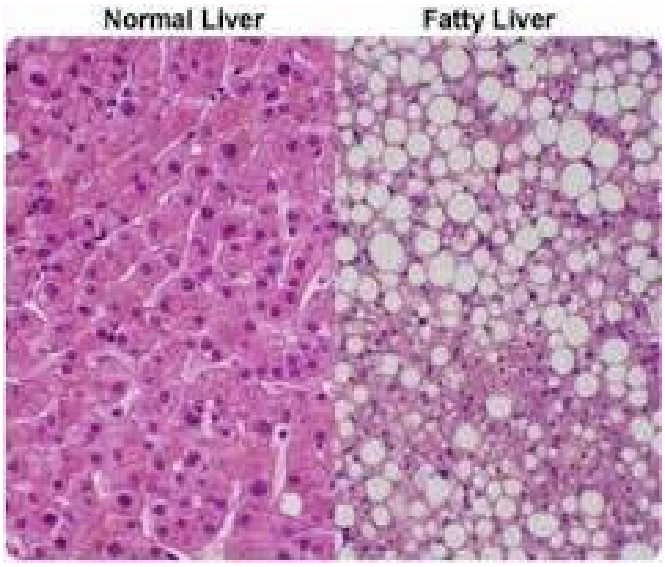
**Figure 4: SPECTRUM OF THE DISEASE[20]**



## FATTY LIVER

- Fatty liver is seen in approximately 90% of the individuals who drink greater than 60g of alcohol per day[21], but may also occur in those who consume less[22]. Patients with uncomplicated fatty liver are usually asymptomatic with a self-limited course, and are reversible completely with abstinence after 4–6 weeks[23]. But, there are studies suggesting the progression to fibrosis and later to cirrhosis can occur in about 5–15% of the patients in spite of abstinence[24,25].

**Figure 5: Histopathology of Liver[17]**




Macrovesicular fat deposits

- On a gross view, the liver is enlarged, yellow, greasy and firm witha smooth and glistening capsule.Microscopic picture of the liver shows microvesicular fat deposits in the cytoplasm initially followed later by macrovesicular deposits displacing nucleus to the periphery.

## ALCOHOLIC HEPATITIS:

- It includes a spectrum of a disease ranging from mild to severe life threatening illness.It usually presents acutely in a background of patients with chronic liver disease.The true prevalence of the disease is not known.Study on the histological slides of the of the patient with ALD suggests as many as 10–35% of hospitalized alcoholic patients have features of alcoholic hepatitis[26,27,28].Symptomatic usually are those with advanced liver disease and concomitant cirrhosis is seen in more than 50% of the patients, with superimposed acute decompensation. As per a study, patients even with a relatively mild presentation are at a high risk for progressive liver injury, with cirrhosis developing in up to 50% of the patients[29, 30], especially in those who continue to abuse alcohol.

# PATHOGENESIS OF ALCOHOLIC HEPATITIS

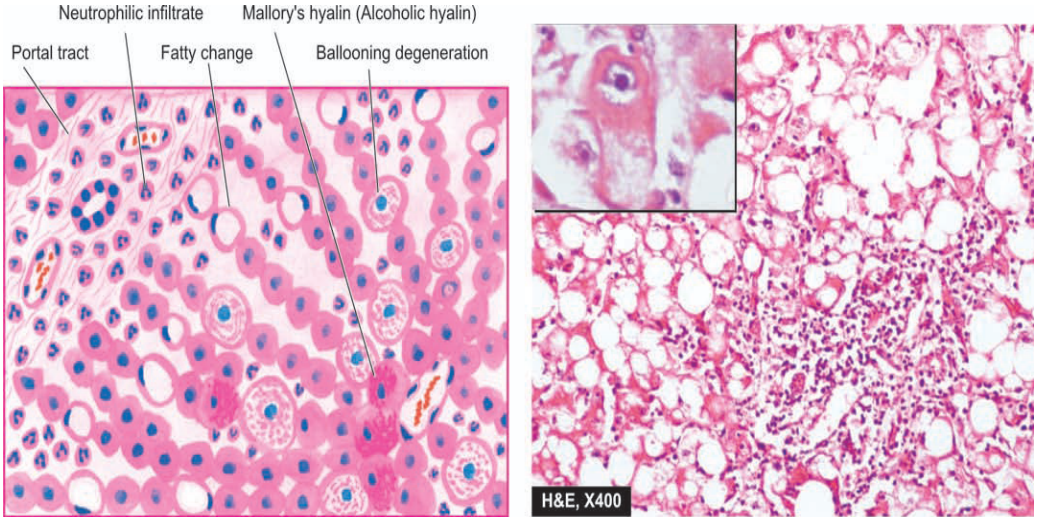



**Figure 6: Histopathology of Alcoholic Hepatitis**[17]

The histological feature of alcoholic hepatitis includes:

- Hepatocellular necrosis with surrounding inflammatory infiltrate, predominantly polymorphs especially in the centrilobular zone. Presence of alcoholic hyaline or Mallory bodies (eosinophilic cytoplasmic inclusions representing aggregates of intermediate filaments-cytokeratin stained by Massons-Trichome or by immune peroxidase method).
- **FIBROSIS:** Most cases are accompanied by fibrosis.

Usually begins in the perivenular[31, 32]and pericellular area producing a web-like or chicken wire like appearance termed as creeping fibrogenesis.

- Alcoholic hepatitis manifests with a wide range of clinical features. Patients symptoms may range from entirely asymptomatic to fever, jaundice and abdominal pain mimicking acute abdomen. Portal hypertension, ascites or variceal bleeding may occur in the absence of cirrhosis. Recognition of clinical features is crucial to the initiation of effective and appropriate diagnostic and therapeutic strategy[10].

**Figure 7: LABORATORY DIAGNOSIS OF ALCOHOLIC FATTY LIVER AND ALCOHOLIC HEPATITIS[10]**

**TABLE 363-2 LABORATORY DIAGNOSIS OF ALCOHOLIC FATTY LIVER AND ALCOHOLIC HEPATITIS**

| Test | Comment |
|---|---|
| AST | Increased two- to sevenfold, <400 IU/L, greater than ALT |
| ALT | Increased two- to sevenfold, <400 IU/L |
| AST/ALT | Usually >1 |
| GGTP | Not specific to alcohol, easily inducible, elevated in all forms of fatty liver |
| Bilirubin | May be markedly increased in alcoholic hepatitis despite modest elevation in alkaline phosphatase |

***Abbreviations:*** ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGTP, γ-glutamyl transpeptidase.

## ALCOHOLIC CIRRHOSIS:

- The term cirrhosis was coined by Laennec in 1818 due to the yellow tawny appearance of the liver due to the presence of fat lobules.It is derived from the greek word *kirrhos=Tawny.* Cirrhosis represents the most severe form of alcohol related liver injury.
- On the gross appearance of the liver in the initial stages shows liver large,fatty weighing more than 2 kg studded with diffuse micronodular nodules(<3cms) resembling a Hob nail pattern (resemblance of the surface with the sole of an old-fashioned shoe having short nails with heads).Later the liver becomes shrunken and non-fatty. Collagen bridges are formed between portal tracts and central veins resulting in isolation of hepatocytes resulting in regenerating macrondular nodules.

**Figure 8: Histopathology of Cirrhosis of Liver**[17]

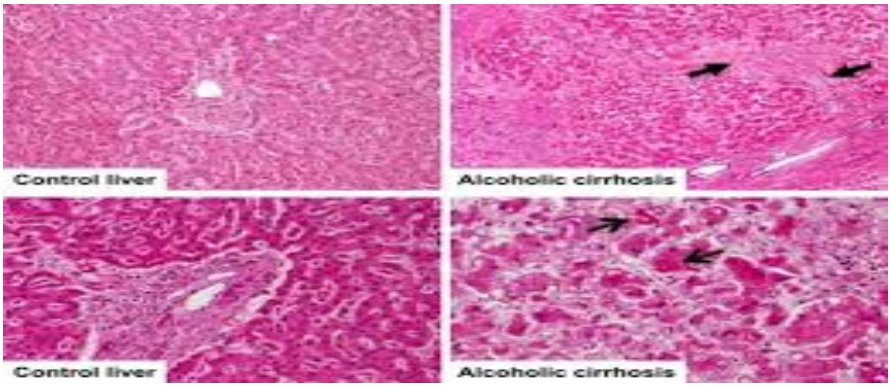



**Figure 9: Clinical Manifestations of Cirrhosis**

**Figure 10: COMPLICATIONS OF CIRRHOSIS**[10]

**TABLE 365-2 COMPLICATIONS OF CIRRHOSIS**

| | |
|---|---|
| Portal hypertension | Coagulopathy |
| Gastroesophageal varices | Factor deficiency |
| Portal hypertensive gastropathy | Fibrinolysis |
| Splenomegaly, hypersplenism | Thrombocytopenia |
| Ascites | Bone disease |
| Spontaneous bacterial peritonitis | Osteopenia |
| Hepatorenal syndrome | Osteoporosis |
| Type 1 | Osteomalacia |
| Type 2 | Hematologic abnormalities |
| Hepatic encephalopathy | Anemia |
| Hepatopulmonary syndrome | Hemolysis |
| Portopulmonary hypertension | Thrombocytopenia |
| Malnutrition | Neutropenia |

## PORTAL HYPERTENSION:

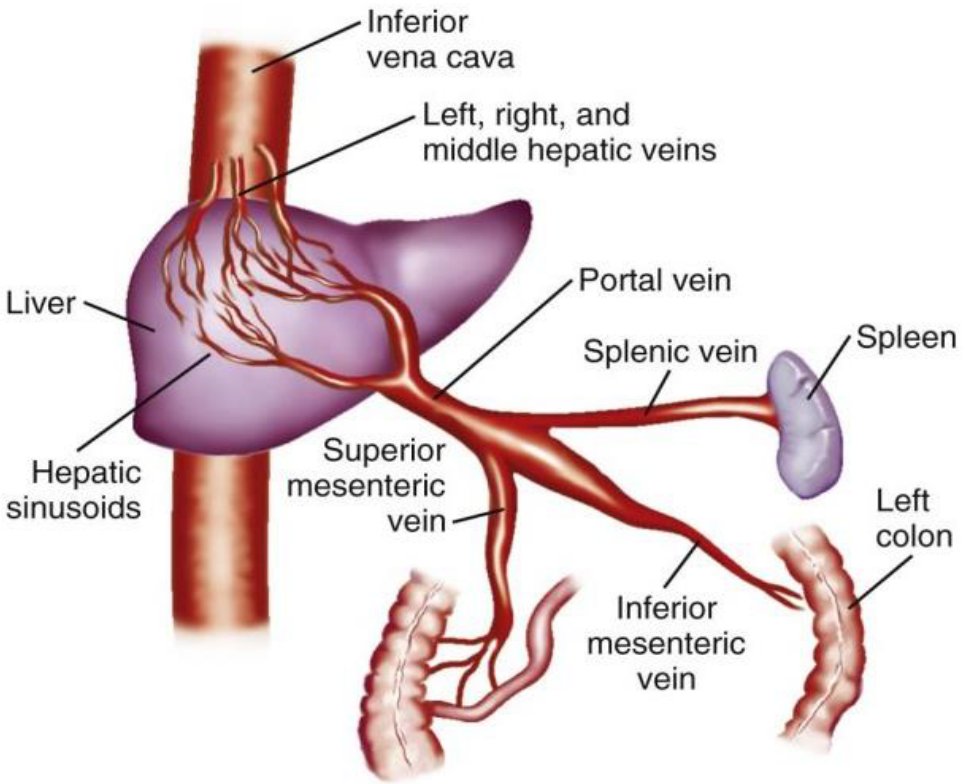
Development of portal hypertension heralds the onset of complications in patients with cirrhosis.

ANATOMY OF THE PORTAL SYSTEM:

- The liver has a dual blood supply from the portal vein and hepatic artery.The portal vein contributes to 2/3$^{rd}$(75%) of the total hepatic blood flow.The portal vein was formed behind the neck of the pancreas atthe confluence of the superior mesenteric vein with the splenicvein at the level of the L2 vertebrae. The length of the main

portal vein ranges from 5.5 to 8 cm and its diameter approximates 1 cm. Portal vein are valveless. The absence of valves in the portal circulation helps to accommodate high flow of blood at low pressure because of the low resistance.This allows for the measurementof portal venous pressure at any point along the system.

**Figure 11: ANATOMY OF PORTAL CIRCULATION**



- Obstruction to the portal flow anywhere along its course results in elevation of portal pressure and portal hypertension.Portal hypertension is defined as the hepatic venous pressure gradient more than 5 mm Hg. Cirrhosis is the most common cause for sinusoidal or intrahepatic hypertension.Clinically significant portal hypertension is defined as a threshold portal pressure gradient of more than or equal to 10 mm Hg as it predicts the best in the development of complications of cirrhosis like ascites.

## PATHOGENESIS OF PORTAL HYPERTENSION:

- It is influenced by two factors.

Increased resistance to $V_S$ Increased splanchnic blood flow.

Intrahepatic blood flow

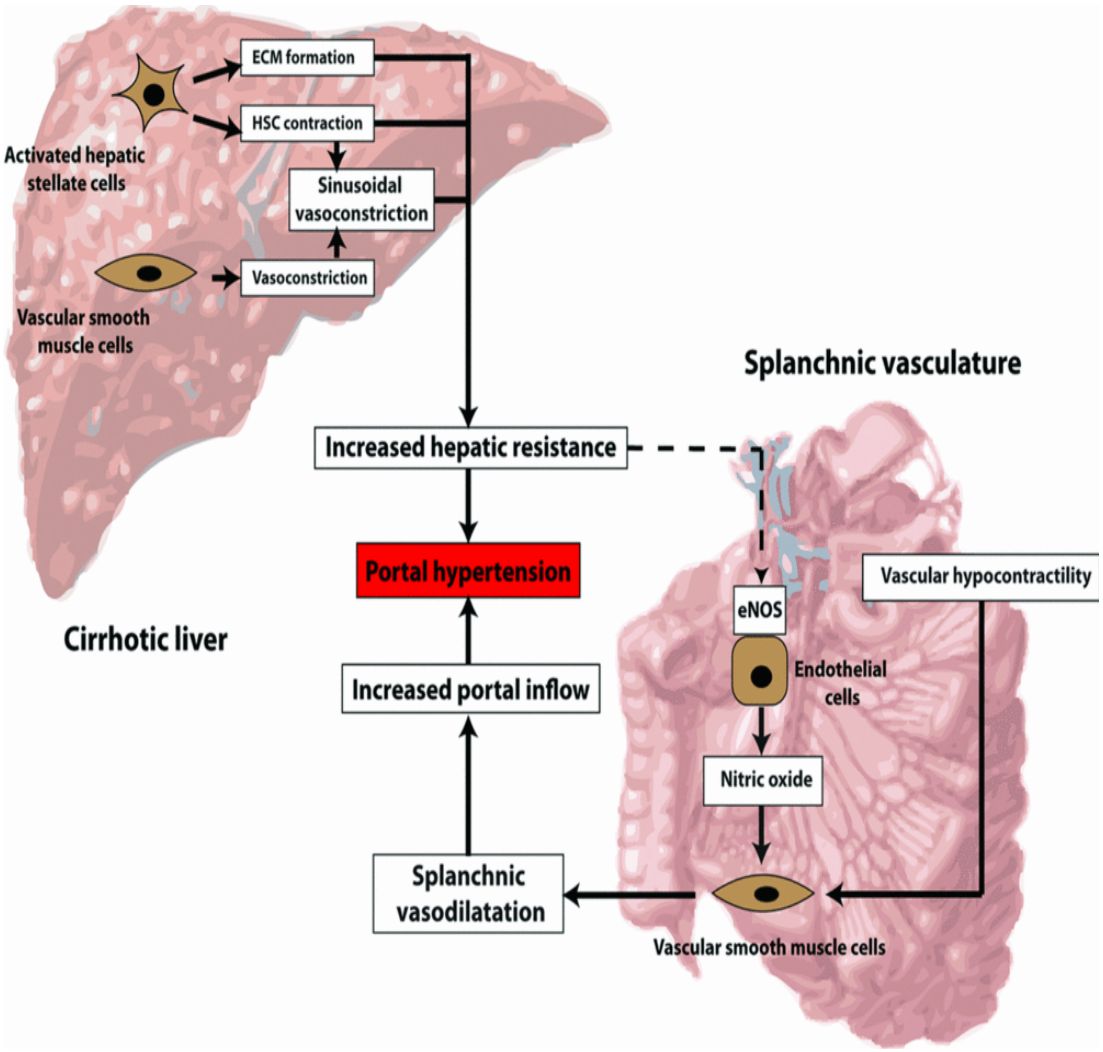
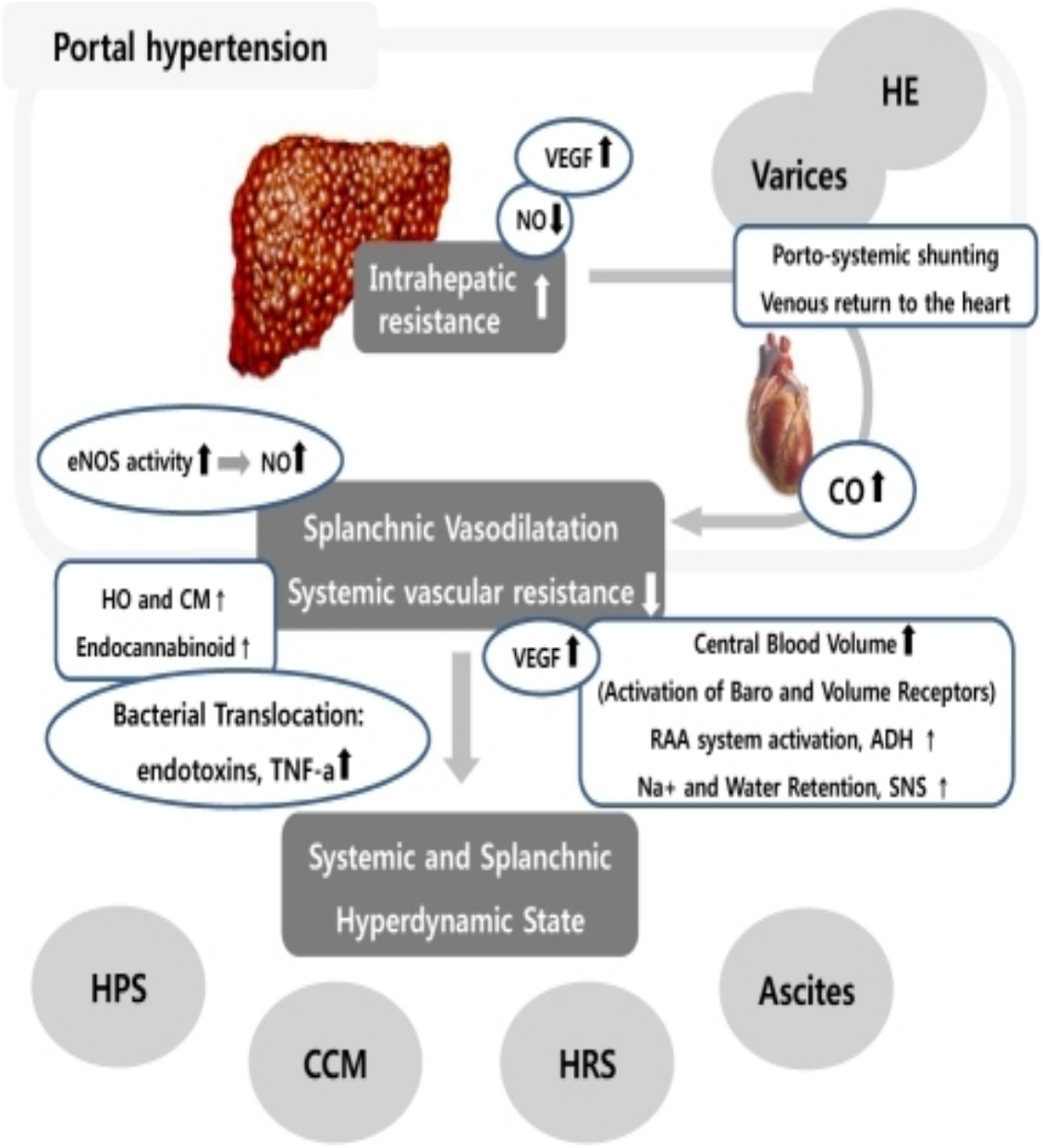



**Figure 11: Pathogenesis of Portal Hypertension**

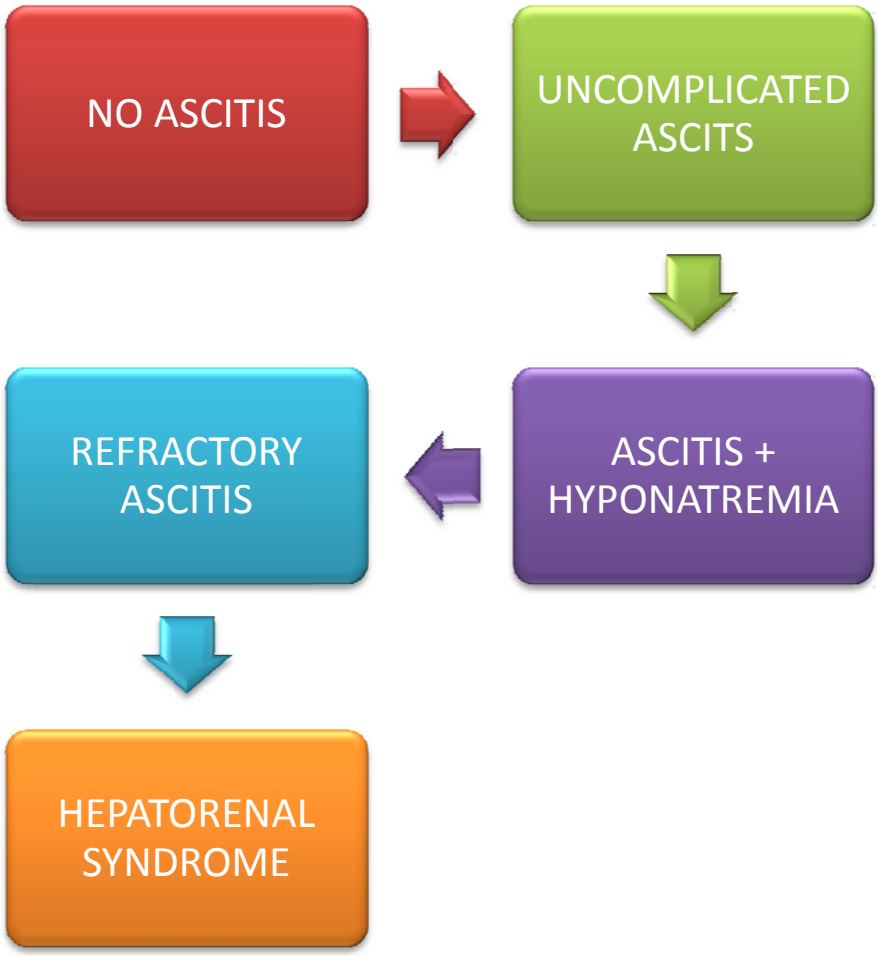
**Figure 12:COMPLICATIONS OF PORTAL HYPERTENSION**



## ASCITIS IN CIRRHOSIS:

- Ascites is the excessive accumulation of fluid in the peritoneal cavity that becomes clinically detectable when it exceeds around 1500 ml.Ascites remains the most common presenting picture of the decompensating event in patient with cirrhosis.Cirrhosis ranks the top in list for ascitis in the western world(75%)[34].

**NATURAL HISTORY OF CIRRHOTIC ASCITIS**



## MECHANISM OF ASCITIC FORMATION IN CIRRHOSIS:

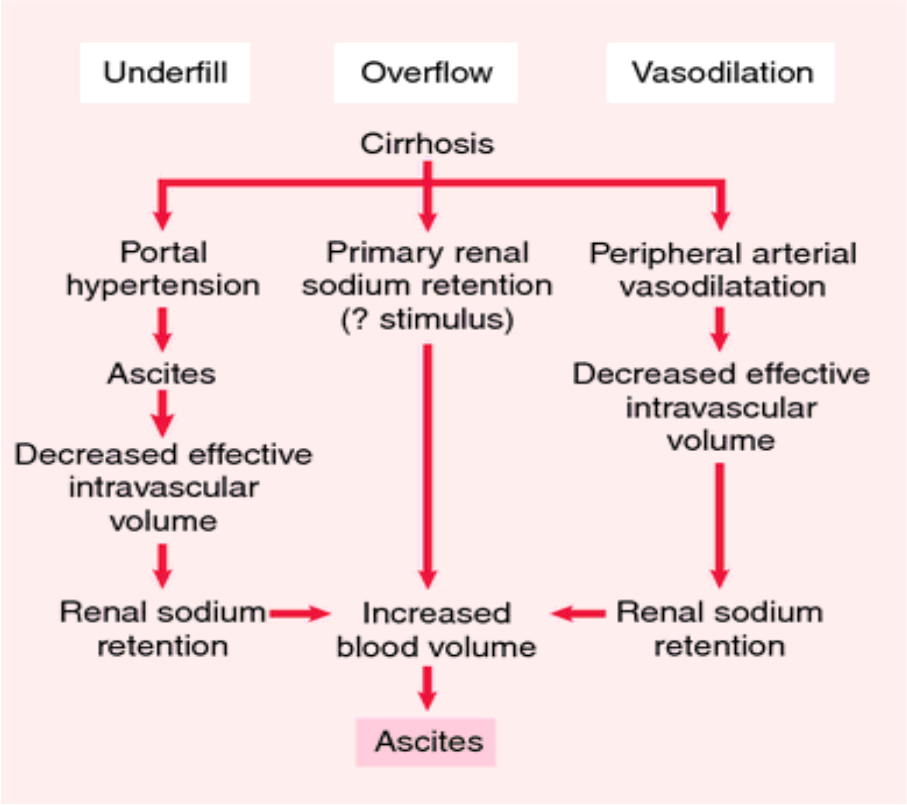
- 2 important factors leading to ascites are sinusoidal hypertension[35, 36] and sodium retention[37].The development of cirrhosis requires a minimum portal pressure gradient of 12 mm Hg[35, 36].

MECHANISM OF ASCITIS IN CIRRHOSIS:

3 THEORIES behind ascites:

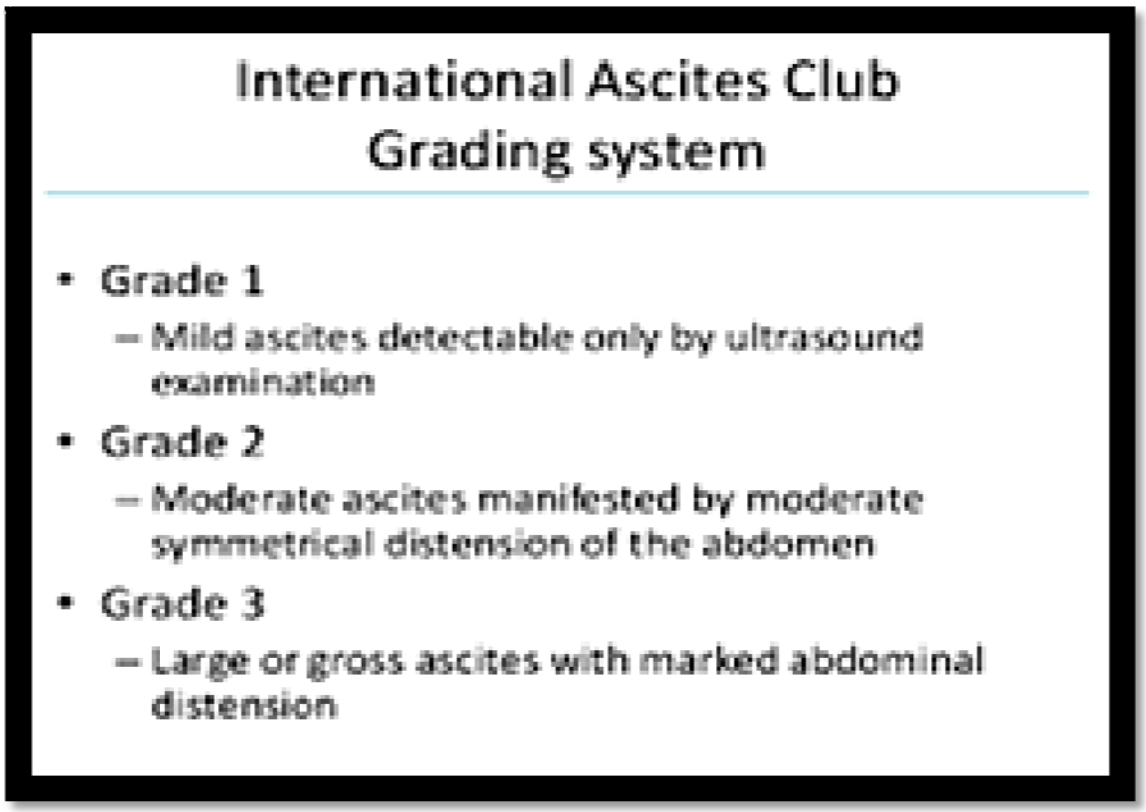
- Underfill theory
- Overfill theory
- Vasodilation theory(most accepted)

**Figure 13: Theory of Ascitis Formation In Cirrhosis**



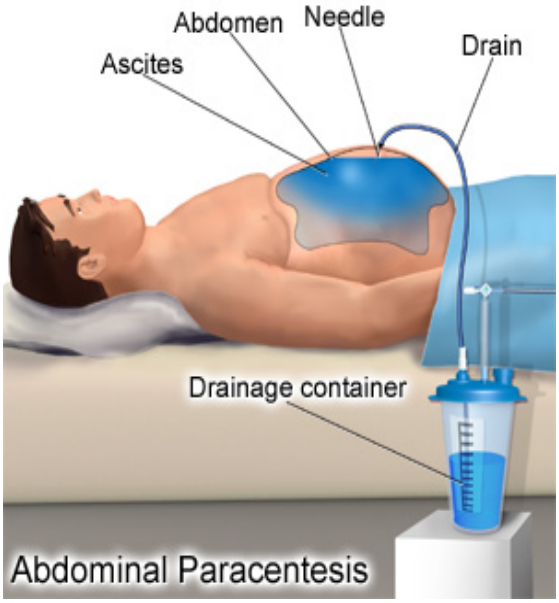
Ascites represents advanced stage of decompensation in patients with cirrhosis.Physical examinations are relatively insensitive especially incase of small ascites and obese patients.1500 ml of fluid is required to become clinically detectable.Shifting dullness remains the most sensitive bedside tool to demonstrate ascites.

**Figure 14: Grading of Ascitis**



- Associated features:
- Umblical hernia due to diastasis of rectus, abdominal and inguinal hernias.Peripheral edema due to hypoproteinemia and functional IVC obstruction due to the mechanical compression of IVC by the fluid.Hydrothorax –seen in 5-10% of the individuals with ascites[39]and is seen as right sided effusion in 85% of the individuals[40, 41] and the mechanism is due to seepage of the ascitic fluid through a diaphragmatic rent.

**Fig.14: Ascitic Fluid Characteristics**



## SPONTANEOUS BACTERIAL PERITONITIS:

- It remains a serious complication of patients with ascites representing infection of ascitic fluid without an intra-abdominal source.It incidence is 30% in patients with ascites and accounts for 25% in hospital mortality.Presence of polymorphs more than 250/U L is required to make a diagnosis ascetic fluid of SBP[38]. Translocation of the gut flora through the intestine into the peritoneal cavity. Most common organisms include E.coli and other gram positive organisms of the gut flora[10]. Culture of the bacteria is negative in 45% of the cases but the yield can be increased by inoculating at the bedside.

REFRACTORY ASCITIS[42]:

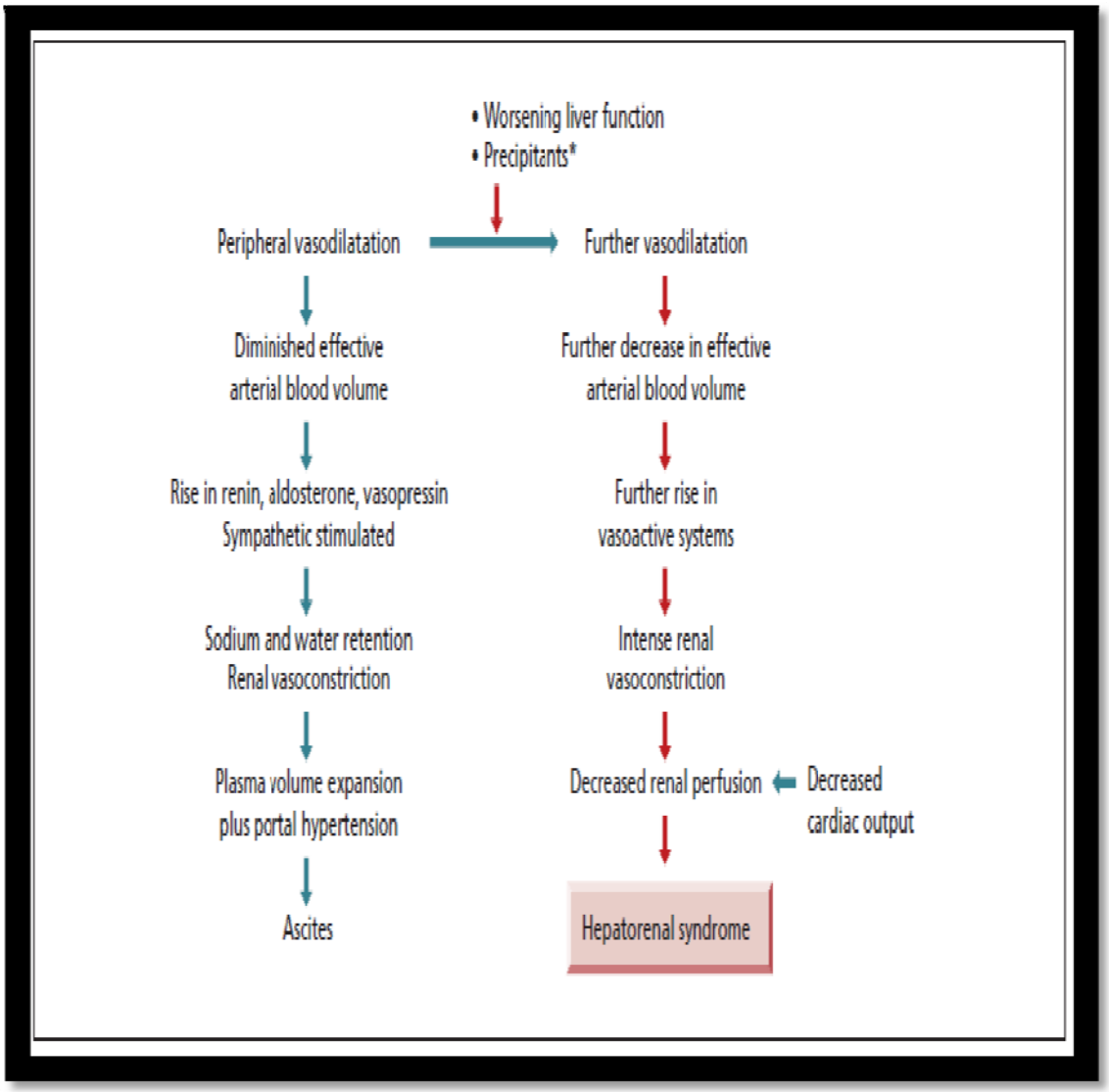
It is defined as that cannot be prevented neither mobilized from recurring by medical therapy.It is of two types:

*diuretic - resistant* (ascites not mobilized inspite of maximal dose of diuretic)

*diuretic – intractable*(presence of complications induced by diuretic that precludes an effective dose of diuretic).

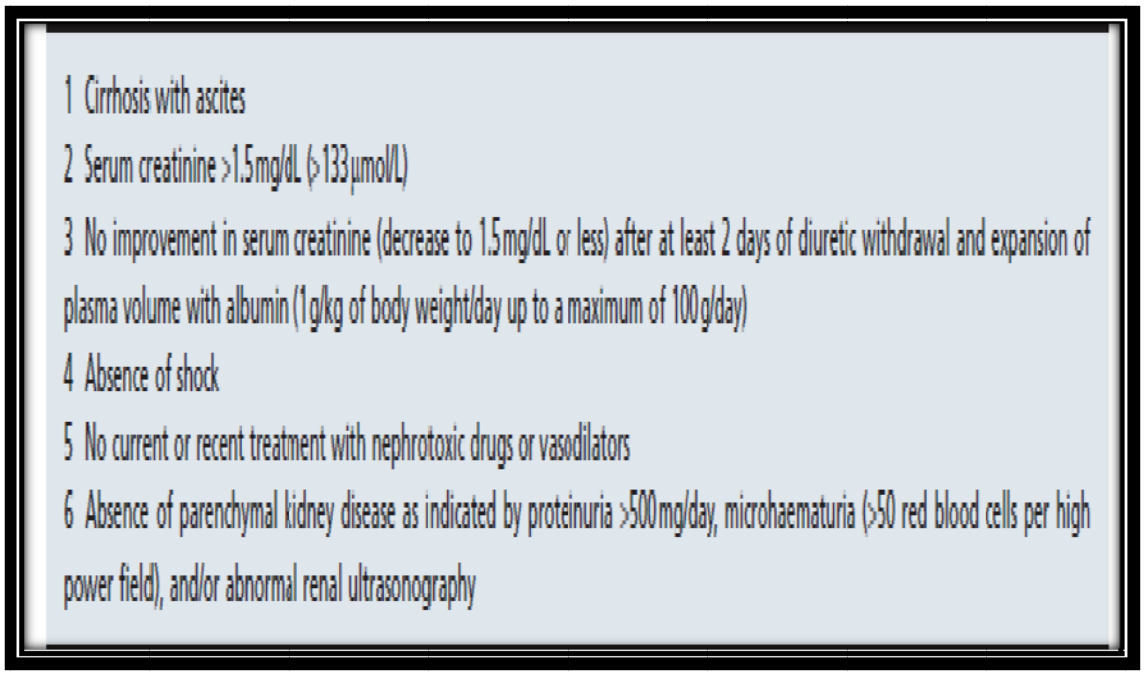
## HEPATO RENAL SYNDROME[43,44]:

**Figure 14: Mechanism of Hepatorenal Syndrome[(45)]**



It's a rare but serious complication with a median survival of 2 weeks.It's a functional rather than a structural abnormality.From the first time of presentation the 5 year incidence of developing HRS is 11% especially its incidence is increased in those with refractory ascitis and in patients with hyponatremia.

**Figure 15: Criteria for Diagnosis of Hepato Renal Syndrome[10]**



## HEPATIC ENCEPHALOPATHY[45]:

Hepatic encephalopathy is the term that is used to describe thecomplex and variable reversible changes in neuropsychiatric status of the patients that complicate the liver disease.Itranges from clinically undetectable changes in the level of cognition to clinically obvious changes in behaviour, motor functions, intellect and consciousness. The exact pathogenesis of portal hypertension syndrome is not known. Porto– systemic shunting and hepatocellular failure remains the chief factors in the development of portal hypertension.Gut – derivedtoxins, such as ammonia escapes from detoxification of liver and impinges on the brain and are detoxified by astrocytes resulting in edema of the brain cells with its ultimate impact on the neuronal function.

**Figure 15: Pathogenesis of Hepatic Encephalopathy**

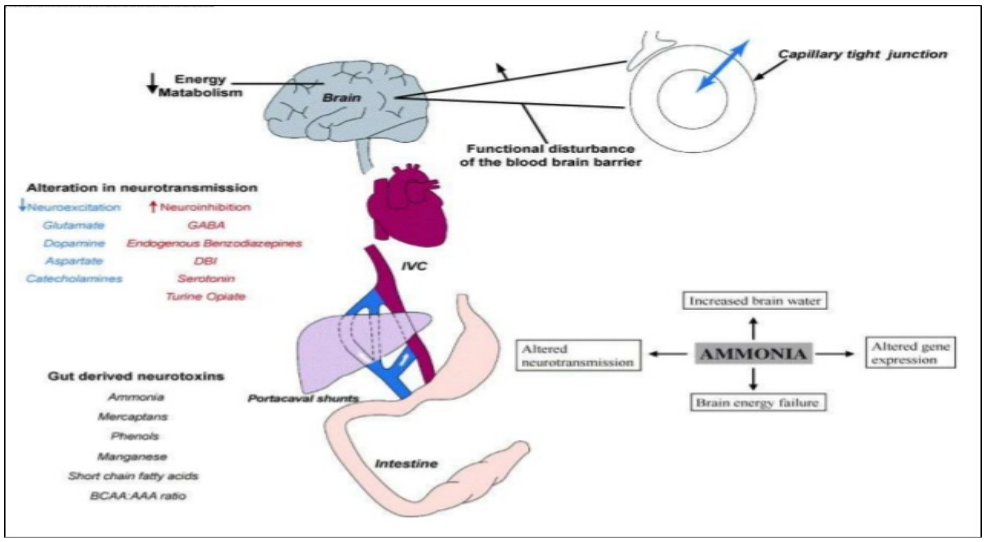


**Figure 16: PRECIPITANTS OF HEPATIC ENCEPHALOPATHY**

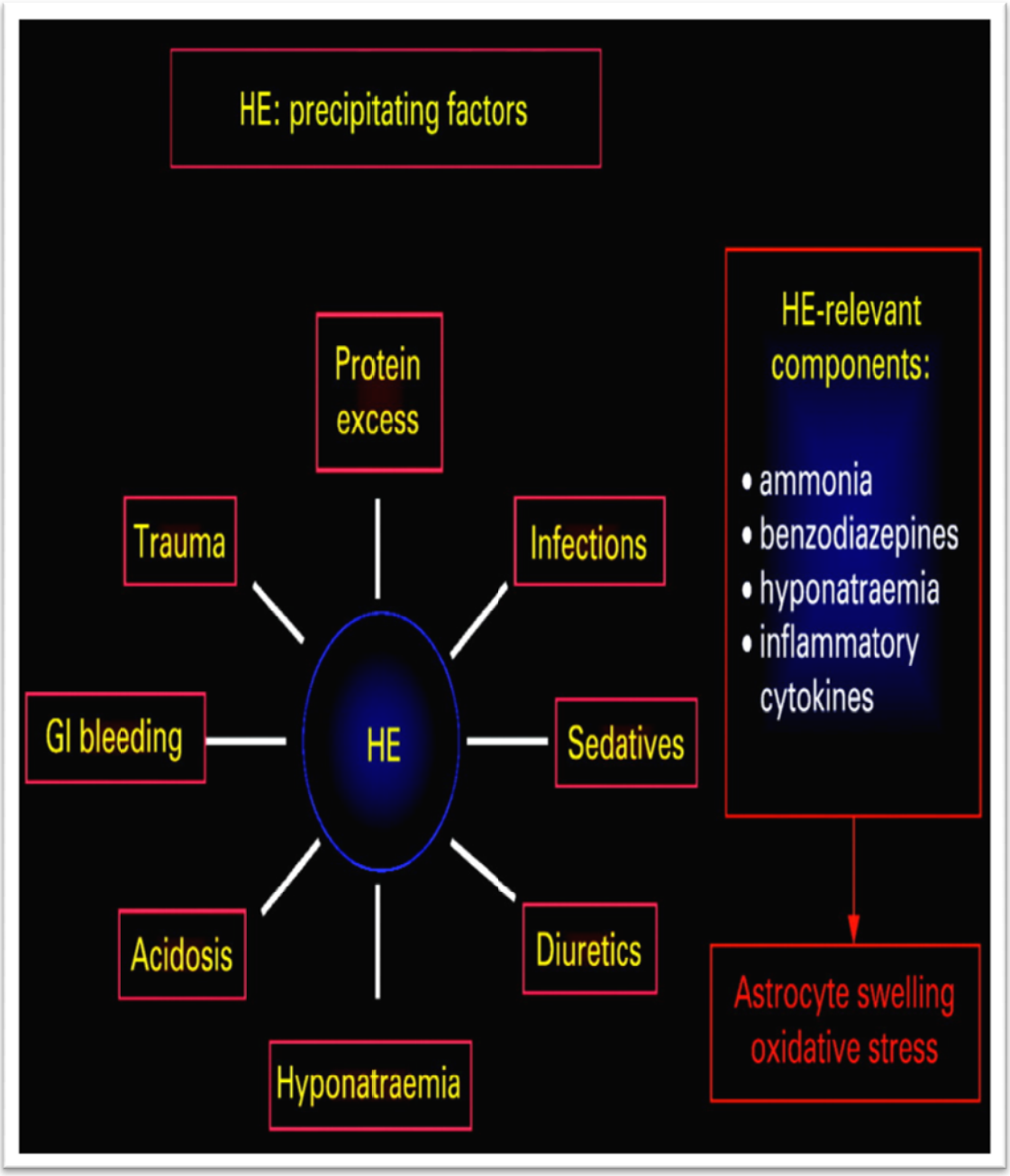
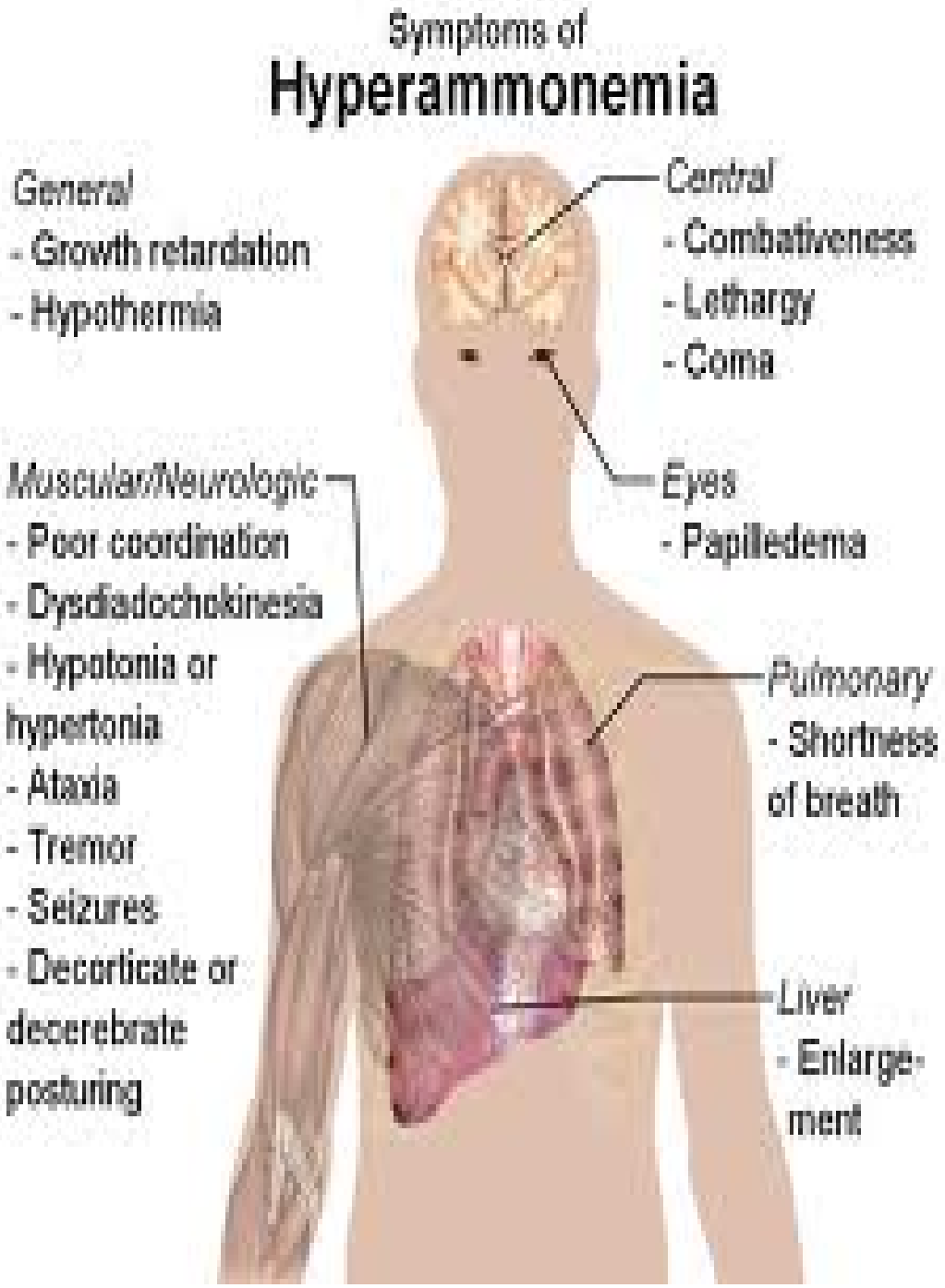


**Figure 17: Symptoms of Hepatic Encephalopathy**

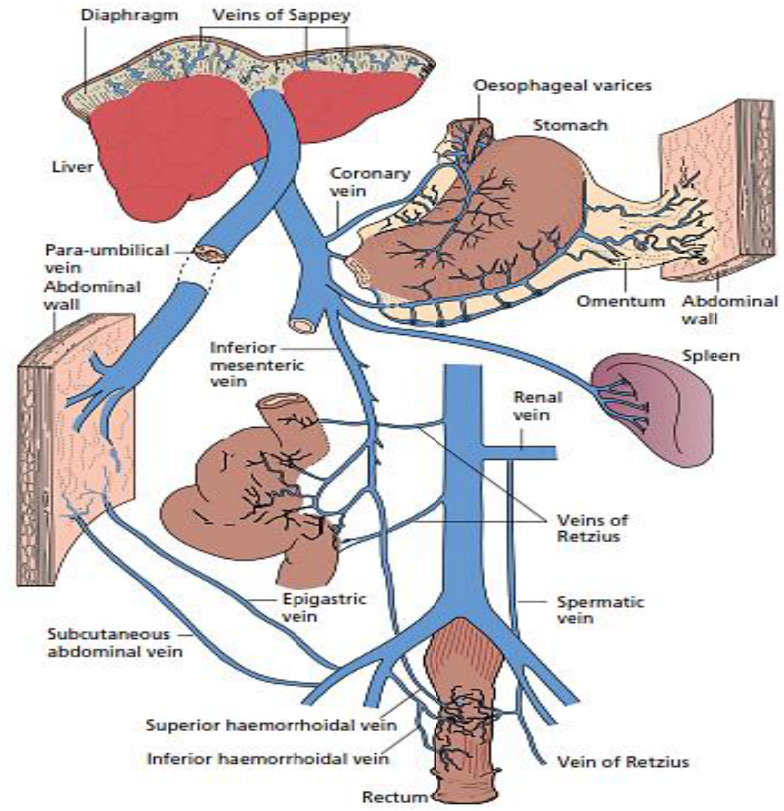


## Figure 18: Grading of Hepatic Encephalopathy

**Table. Grading of Hepatic Encephalopathy**

| Grade | Level of Consciousness | Personality and Intellect | Neurologic Signs | Electroencephalogram (EEG) Abnormalities |
|---|---|---|---|---|
| 0 | Normal | Normal | None | None |
| Subclinical | Normal | Normal | Abnormalities only on psychometric testing | None |
| 1 | Day/night sleep reversal, restlessness | Forgetfulness, mild confusion, agitation, irritability | Tremor, apraxia, incoordination, impaired handwriting | Triphasic waves (5 Hz) |
| 2 | Lethargy, slowed responses | Disorientation to time, loss of inhibition, inappropriate behavior | Asterixis, dysarthria, ataxia, hypoactive reflexes | Triphasic waves (5 Hz) |
| 3 | Somnolence, confusion | Disorientation to place, aggressive behavior | Asterixis, muscular rigidity, Babinski signs, hyperactive reflexes | Triphasic waves (5 Hz) |
| 4 | Coma | None | Decerebration | Delta/slow wave activity |

## Figure 19: Sites of Porto Systemic Collaterals



## PORTO-SYSTEMIC COMMUNICATION:

There are numerous connections between the portal andsystemic venous systems. Under conditions of high portal venous pressure, these porto-systemic connections may enlarge secondarily to collateral flow.

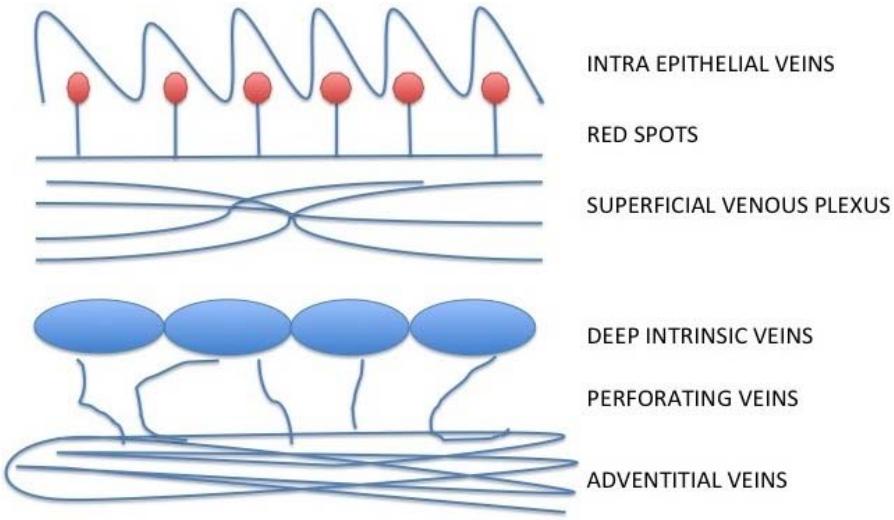
The development of porto-systemic collaterals in case of portal hypertension leads to two basic mechanism:

(1) neo-angiogenesis and

(2) dilatation of embryonic channels that are pre existing between the portal and systemic circulations[27, 28].

Esophageal Varices are abnormally engorged submucosal veins in the lower part of esophagus. Variceal haemorrhage is a life-threatening complication seen in cirrhosis that develops once the HVPG exceeds 12 mm Hg.The major blood supply of esophagus is from the left gastric vein.The diameter normally is 1 mm which raise to 1-2 cms during portal hypertension.

**Figure 20: LAYERS OF ESOPHAGUS[45]**




The intra epithelial veins are seen as red spots in endoscopy. The trunk arising from adventitial plexus serves as the source of large esophageal varices. A common site for oesophageal variceal rupture to occur is at the Gastro-esophagealjunction at the palisade zone – an area between the perforating zone of the oesophagus and the gastric zone).This area serves as a watershed area between the portal veins and the azygous, here the flow is bidirectional resulting in a turbulent flow leading to rupture frequently.

After the initial diagnosis of cirrhosis the yearly risk of developing varices is 5-8% /year[49, 50].

Two determining factors for the development of varices include

1. Ongoing liver injury by the continuous use of alcohol and
2. The severity of porto-systemic connections[51].

The annual rate of increase in the size of varices from small to large is 10-15%. Inspite of the high prevalence only 30% of the patients will bleed. Risk of UGI bleed is greatest at the first year of diagnosis with a high mortality rate of 30%-50% at the first episodes.

**Figure 21: A COMPARITIVE ANALYSIS OF THE DIFFERENT GRADING OF ESOPHAGEAL VARICES**

| Japanese | US | VA Trial | Paquet |
|---|---|---|---|
| Absent | Absent | Absent | I |
| Grade 1: small, straight varices not disappearing with insufflation | smal | < 5 mm | II |
| Grade 2: medium varices occupying less than one third of the lumen | mediu m | 5-9 mm | III |
| Grade 3: large varices occupying more than one third of the lumen | large | > 9 mm | IV |

## ENDOSCOPY

**Figure 22: History of Endoscopy**

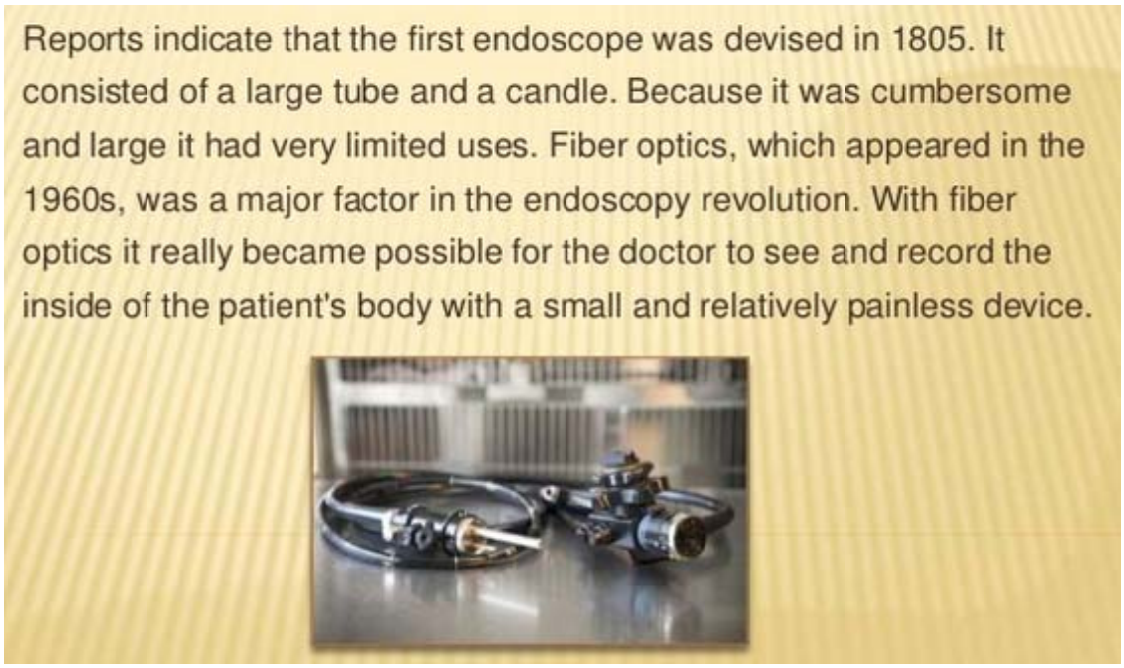
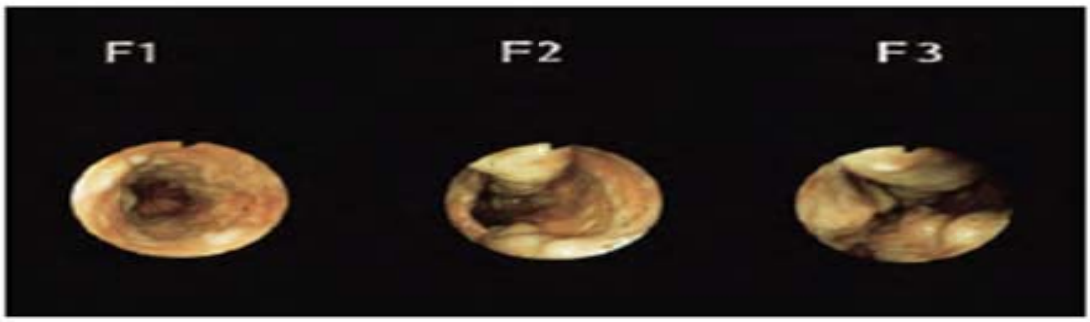



**Figure 23: Grades of Varices on Endoscopy**[45]

COMPLICATIONS OF ENDOSCOPY:

The use of endoscopy has increased greatly in the recent years but has its own risk.Adverse events due to endoscopic procedures become unacceptable if endoscopy is not indicated.

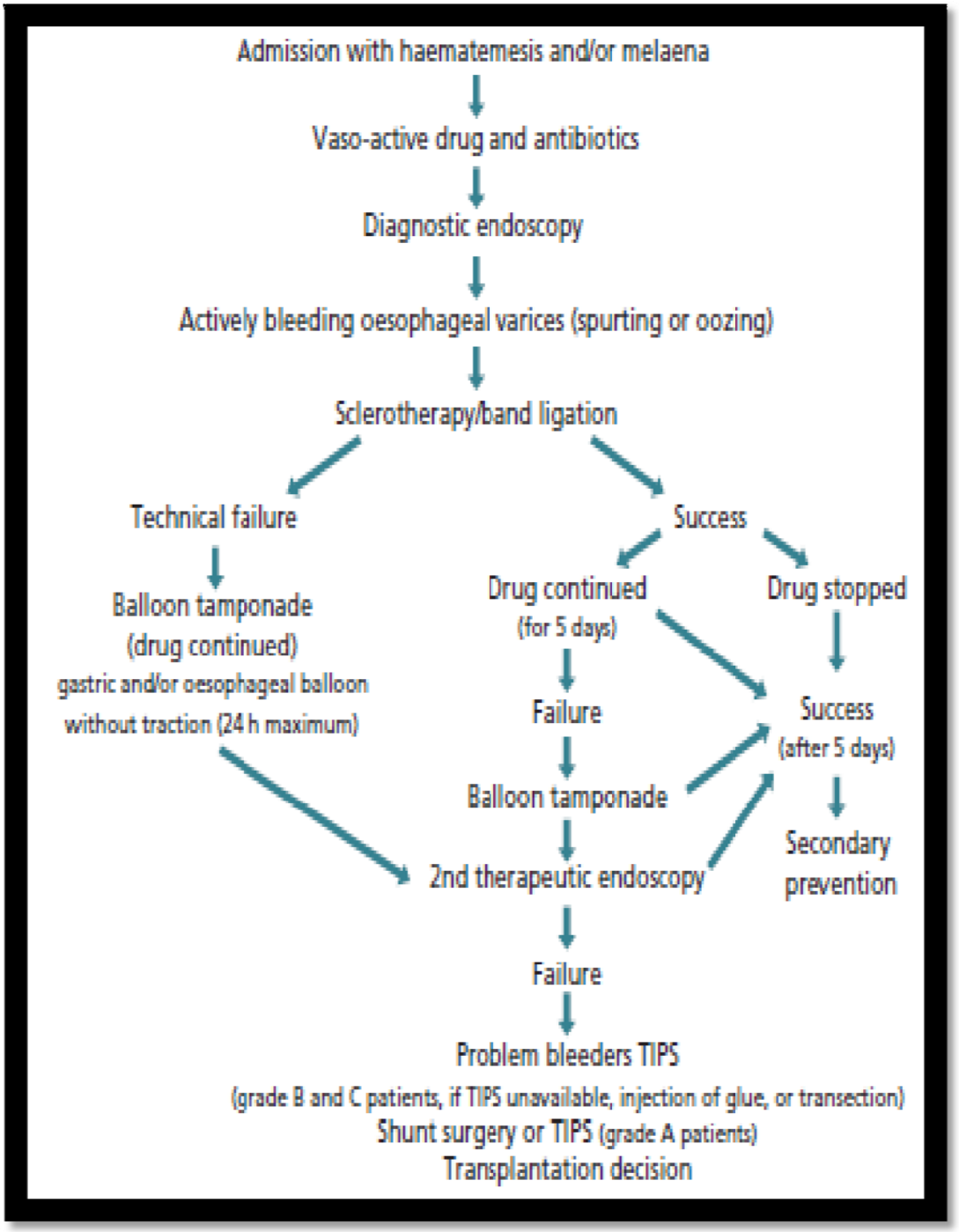
- "National Confidential Enquiry into Patient Outcome and Death report"-"scoping our practice"[48] analyzed death that occurred in UK within 30 days of endoscopy done for therapeutic procedure.
- "scoping our practice" viewed 1818 therapeutic endoscopies in 263 patients with an analysis of events that related to complications and death.
- They highlighted various inadequacies that resulted in complication and stated that there should be national guidelines to guarantee competent endoscopy.

COMPLICATIONS OF ENDOSCOPY:

- Risk of rupture of the organs
- Risk of bleeding
- Infections
- Anesthesia related complications
- Patients' compliance.

This has lead to consensus in the search for various non- endoscopic indicators to predict varices and its risk of bleeding in patients with cirrhosis.

**Figure 24:Approach to a Patient with UGI Bleed**[45]



**CHILD –PUGHS SCORE**:

Dr. C.G. Child and Dr. J.G. Turcotte of the University of Michigan in 1964[52]first proposed a system for scoring inorder to estimate the surgical risk in patients recovered from UGI bleed who are candidates for porto-systemic shunt. They considered 5 variables out of clinical experience: serum levels of albumin and bilirubin,ascites,hepatic encephalopathy and nutritional status and classified as best (A), moderate (B), or worse (C) prognosis.

**Figure 25: Dr. J.G. Turcotte**

- In 1973, Pugh *et al*. [53] modified this version by replacing nutritional status with prothrombin time (PT) and gave a score of 1 to 3 to each variables.

- Child-Pugh classification is the most commonly used scoring system to evaluate the prognosis of patients with cirrhosis of liver[54].
- Two out of the fivevariables were subjective, while the rest of the three were laboratory.

**Figure 26: Child Pugh Score[10]**

## Child-Pugh Classification of Cirrhosis

| Factor | Units | 1 | 2 | 3 |
|---|---|---|---|---|
| Serum bilirubin | mol/L<br>mg/dL | <34<br><2.0 | 34-51<br>2.0-3.0 | >51<br>>3.0 |
| Serum albumin | g/L<br>g/dL | >35<br>>3.5 | 30-35<br>3.0-3.5 | <30<br><3.0 |
| Prothrombin time | seconds prolonged<br>INR | 0-4<br><1.7 | 4-6<br>1.7-2.3 | >6<br>>2.3 |
| Ascites | | None | Easily controlled | Poorly controlled |
| Hepatic encephalopathy | | None | Minimal | Advanced |

The Child-Pugh score is calculated by adding the scores of the five factors and can range from 5 to 15. Child-Pugh class can be A (a score of 5-6), B (7-9), or C (10 or above). Decompensation indicates cirrhosis with a Child-Pugh score of >7 (class B).

- Child Pugh calculation is a simple bedside prognostic measures in patients with alcoholic cirrhosis.It is a good predictor of outcome in patients with complications of portal hypertension.It predicts the 1 yr and 2 yr mortality in patients with alcoholic cirrhosis.

In patients with cirrhosis,the 1yr and 2 yr mortality were found to be

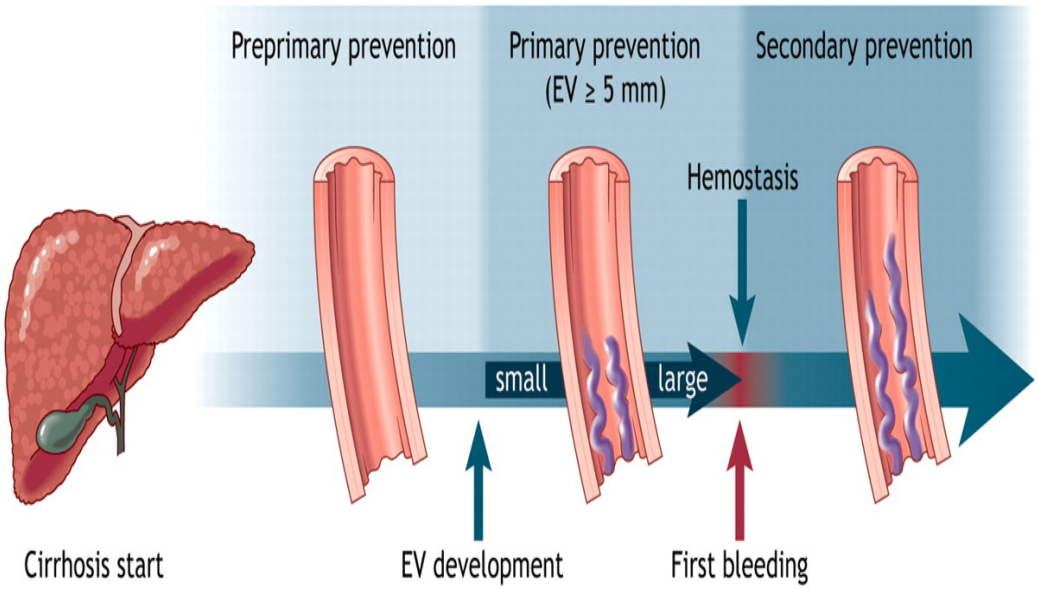
- Child Pugh class A(well compensated cirrhosis)-100 and 85% respectively.
- Child Pugh class B(significant functional compromise) -80 and 60% respectively.
- Child Pugh class C(decompensated)-45 and 35% respectively.

Currently, numerous studies are published with the utility of Child Pugh score - A few mentioned below

- To select the patients pre operatively for liver transplantation.
- To assess for the hepatic resection in Patients with hepatocellular carcinoma.
- Prognosis of the patients with hepatocellular carcinoma planned for radiotherapy.

- To predict for the presence of esophageal varices and its severity and the risk of rebleed.

**Figure 27: Primary Prophylaxis of Esophageal Varices**




- Our current approach should be targeted towards the preprimary prevention of the disease to prevent the dreaded complication of rupture of the varices that accounts for a significant mortality in patients with alcoholic cirrhosis.
- Several studies are targeting to tackle the problem,by the search for parameters other than the invasive endoscopic procedure to target at the grassroot level.

- Clinical laboratory and non invasive parameters are under study, in search for effective non-endoscopic parameters for the presence of varices.
- Child-Pugh score to assess the prognosis and mortality of the patients with alcoholic cirrhosis are now under study in the usefulness of the score to assess the severity and the presence of varices.

# 4. MATERIALS& METHODS

## *DESIGN OF STUDY*

Time period of study – March 2015 to August 2015(6 months)

Age of patients - 18 years and above

Gender of patients –Both Males& Females

Place – Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai.

## *INCLUSION CRITERIA*

Age – 18 years or more

Patients with alcoholic liver disease(Associated with significant intake of alcohol)

## *EXCLUSION CRITERIA*

- Pregnancy.
- Age <18 years.
- Patients with liver disease due to causes other than alcohol(Infection, NASH, other hepatotoxins, etc.)

- Patients with alcoholic liver disease with previous history of varices, or upper gastro intestinal bleed or any therapeutic intervention for the same.
- Patients with upper gastrointestinal bleed with no significant alcohol intake.
- Patients with hematological disorders or patients on drugs(anti-platelets, anti-coagulants or hepatotoxic drugs).
- Patients with alcoholic liver disease with gastric varices.
- Patients who were treated with b blockers either currently or in the past.

## ***SAMPLE SIZE***

The samples selected for this study were patients who came for treatment at Madras Medical College and Rajiv Gandhi Government General Hospital for alcoholic liver cirrhosis. Study group/study population was the number of patients had alcohol induced liver disease and on further evaluation and management in the Department of General Medicine, Madras Medical College and Rajiv Gandhi Government General Hospital. The sample size of 106 was calculated by analyzing with Power analysis test

with the prevalence rate of alcoholic liver disease as 20% in south India and found to be statistically significant[2].

## ***ETHICS***

The study was performed after the approval of the institutional ethics committee of Madras Medical College and Rajiv Gandhi Government General Hospital. The procedure was performed in accordance with the ethical standard and photographs were taken with patients and their relatives' full consent.

## ***INFORMED CONSENT***

All patients were enrolled into the study after getting informed & written consent. Proforma of informed& written consent is enclosed in annexure III.

The essence of consent comprised of the following:

- Consent explaining risks and benefits of the study and need for UGI endoscopy in the evaluation of the disease (To assess oesophageal varices in Alcoholic liver disease).

- Also explaining that UGI endoscopy may just be an aid in diagnosis, not a manner in which the problem can be entirely fixed or cured.

## ***DATA RECORDING***

Records from all the patients in the study group was collected and documented in the proforma framed for this study. Proforma used is attached as annexure I.

**All Patients in the study were subjected to,**

- In the study all the patients underwent a detailedhistory taking using the AUDIT Questionnaire(attached in annexure II). Though different questionnaires are available, AUDIT questionnaire had higher reliability.This 10 points questionnaire was proposed by WHO to avoid the ethnical and cultural bias. Patients with significant alcohol intake are included in the study after the history. Though the significant level of alcohol to cause the damage is not well

established,most of the researches signifies that the consumption of >30 g/day of alcohol is significant that is utilized in this study[55].

- Physical examination
- Laboratory tests –Complete Hemogram, BT/CT/PT/INR, Blood Grouping, Liver Function Test, S. Albumin.
- Non invasive imaging USG and Doppler
- Upper Gastro intestinal endoscopy
- Child Pugh score assessmentfor all patients

## Child-Pugh Classification of Cirrhosis

| Factor | Units | 1 | 2 | 3 |
|---|---|---|---|---|
| Serum bilirubin | mol/L<br>mg/dL | <34<br><2.0 | 34-51<br>2.0-3.0 | >51<br>>3.0 |
| Serum albumin | g/L<br>g/dL | >35<br>>3.5 | 30-35<br>3.0-3.5 | <30<br><3.0 |
| Prothrombin time | seconds prolonged<br>INR | 0-4<br><1.7 | 4-6<br>1.7-2.3 | >6<br>>2.3 |
| Ascites | | None | Easily controlled | Poorly controlled |
| Hepatic encephalopathy | | None | Minimal | Advanced |

The Child-Pugh score is calculated by adding the scores of the five factors and can range from 5 to 15. Child-Pugh class can be A (a score of 5-6), B (7-9), or C (10 or above). Decompensation indicates cirrhosis with a Child-Pugh score of >7 (class B).

## ***TECHNIQUE ADOPTED***

- Child Pugh Score Calculation for every patient and Comparison with UGI endoscopy findings of them.
- Comparing other physical findings, blood and imaging parameters with the UGI endoscopy findings to assess its significance in the study conducted.
  - Physical findings – Pallor, Icterus, Spider naevi, Hepatic encephalopathy, Ascitis, Splenomegaly.
  - Blood Investigations – Hemoglobin, Platelet count, Total Bilirubin, S. albumin, INR (INR considered for comparison in my study instead of Prothrombin time prolongation, both for individual parameter comparison and for calculating Child Pugh Score because it is to be more reliable and standardized test comparing to Prothrombin time).
  - Ultrasonogram – liver and spleen size, Portal Vein diameter, ascitis.

## STATISTICAL DATA ANALYSIS

For this study, historical, clinical,laboratory, endoscopic data and Child Pugh score charts were documented for all the 106 subjects under study, in the form of a proforma and computed into Microsoft excel spreadsheets and coded. All results were analyzed using SAS 9.2, SPSS 15.0 which are commercially available statistical softwares. Descriptive and inferential statistical analysis had been carried out in the present study. Results on continuous measurements were presented as Mean $\pm$ SD (Min-Max) and results on categorical measurements were presented in Number (%). Significance was assessed at 5% level of significance. Independent sample test and paired sample T test (ANOVA) has been used to find the significance of study parameters on categorical scale between two or more groups after checking for normal distribution of all variables.

## LIMITATIONS

- Single center study may not reflect the general population,
- Possibility of observational bias in upper GI endoscopy and imaging since they were operator dependant.

# 5. OBSERVATION

Total number of cases : 106

Parameters Studied :

- Age and gender epidemiological parameters.
- Significance of the Child Pugh Score and its association with the evaluation of Esophageal varices.
- Various Clinical features analyzed with esophageal varices.
- Association of Laboratory parameters with esophageal varices.
- Significance of USG measurement of Portal vein diameter with esophageal varices.

All the above details were analyzed and tabulated in the master worksheet for comparison between individual cases and with published data.

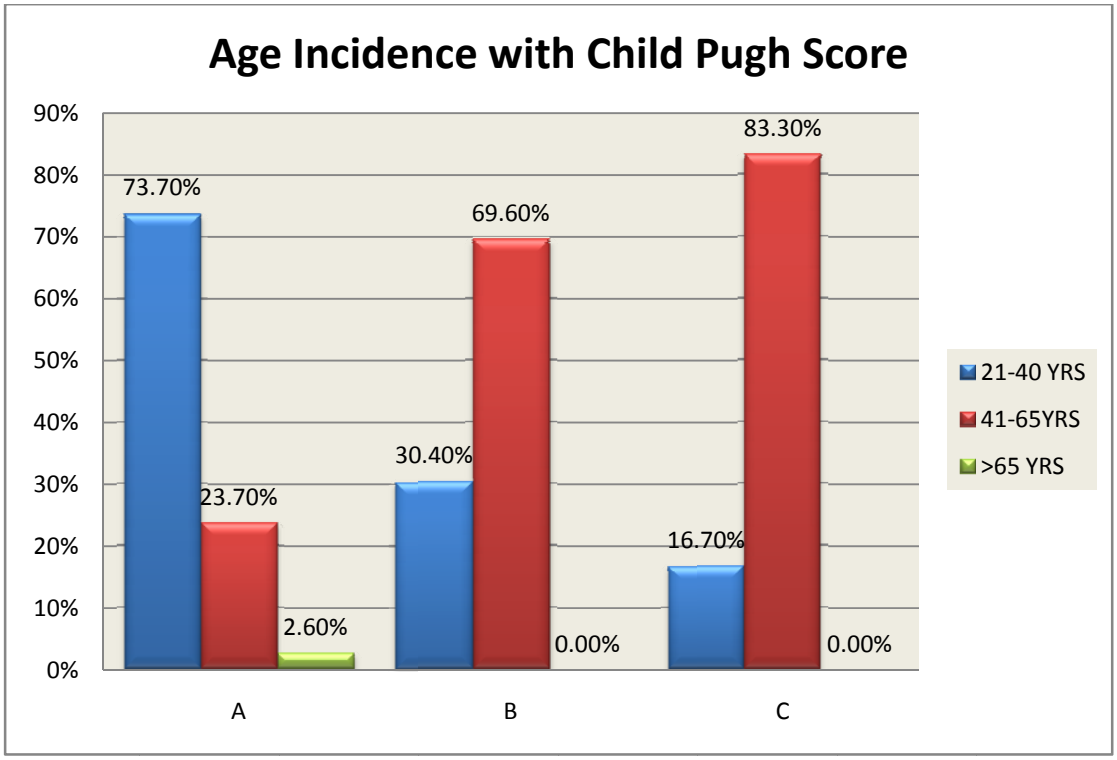
## ***AGE AND SEX INCIDENCE***

Out of 106 patients studied, 44.4% were in the age group of 21 to 40 years (Young adults) and 54.7% were in the middle age (41- 65 years) and 0.9% belonged to senior citizens (> 65 years)[56]. And 35.8% belong to Child Pugh Score A and 52.8% belong to Child Pugh Score B and 11.4% belongs to Child Pugh Score C category.

**Table 1: AGE INCIDENCE WITH CHILD PUGH SCORE**

| Age | Child Pugh Score A | Child Pugh Score B | Child Pugh Score C | Total |
|---|---|---|---|---|
| Young Adults (21 – 40) | 28(59.6%) | 17(36.2%) | 2(4.2%) | 47(44.4%) |
| Middle age (41 – 65) | 9(15.5%) | 39(67.2%) | 10(17.3%) | 58(54.7%) |
| Old age (≥ 65) | 1(100%) | 0(0%) | 0(0%) | 1(0.9%) |
| Total | 38(35.8%) | 56(52.8%) | 12(11.4%) | 106 |

In our study of 106 patients, most of the patients falls under middle age group of 41-65 years(54.7%).majority of the patients belong to Child Pugh score B(52.8%).

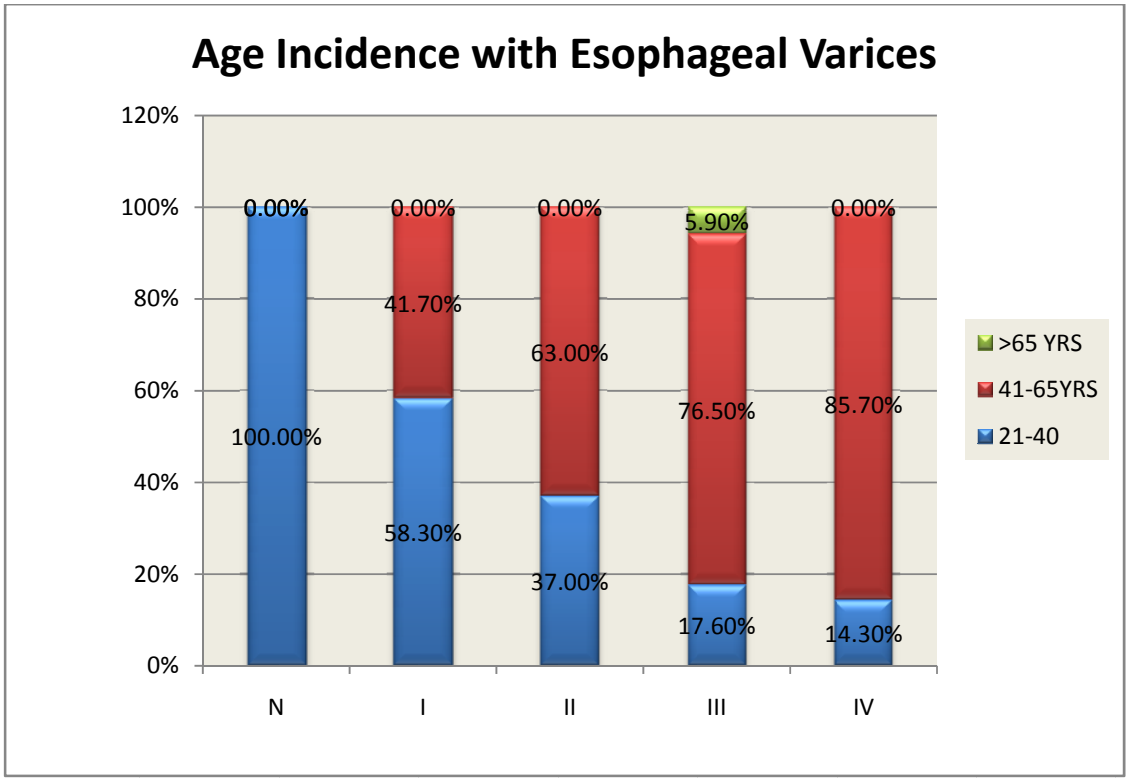



**AGE INCIDENCE CHART WITH ESOPHAGEAL VARICES**

**Table 2: AGE INCIDENCE WITH ESOPHAGEAL VARICES**

| Age | NO | I | II | III | IV | TOTAL |
|---|---|---|---|---|---|---|
| Young Adults (21 – 40) | 12(25.5%) | 14(29.8%) | 17(29.8%) | 3(6.4%) | 1(2.1%) | 47 (44.4%) |
| Middle age (41 – 65) | 0(0%) | 10(17.2%) | 29(50%) | 13(22.4%) | 6(10.3%) | 58 (54.7%) |
| Old age (≥ 65) | 0(0%) | 0(0%) | 0(0%) | 1(100%) | 0 | 1(0.9%) |
| | 12(11.3%) | 24(22.6%) | 46(43.4%) | 17(16%) | 7(6.7%) | 106 |

Majority of the patients in the study (66%) had small varices of Grade I-II.




In the study, majority of the patients with large varices falls under middle (41-65 years)and elderly(>65 years) age group.

| Table 3: AGE DISTRIBUTION | | | | | |
|---|---|---|---|---|---|
| | N | Minimum | Maximum | Mean | Std. Deviation |
| Age_in_years | 106 | 25.00 | 68.00 | 43.2075 | 10.40761 |

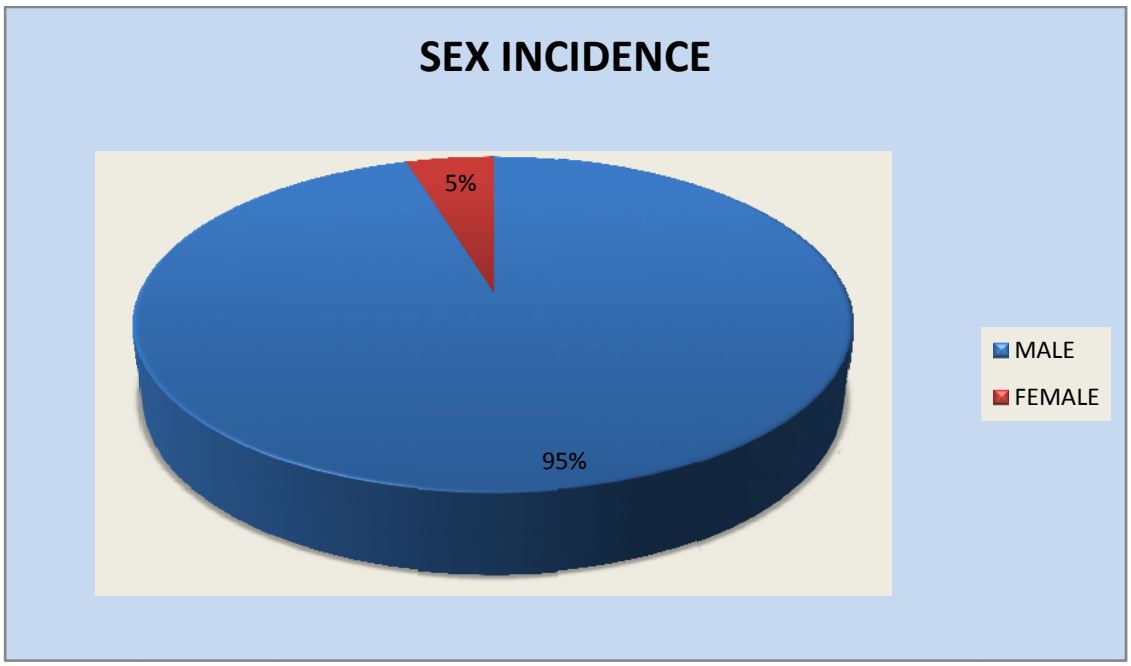
The mean age group of our study population is 43.2 years.

## ***SEX INCIDENCE***

In the study population of 106, males were 101 attributing to 95.3% and females were 5 contributing to only 4.7%.

**Table 4: Sex Distribution**

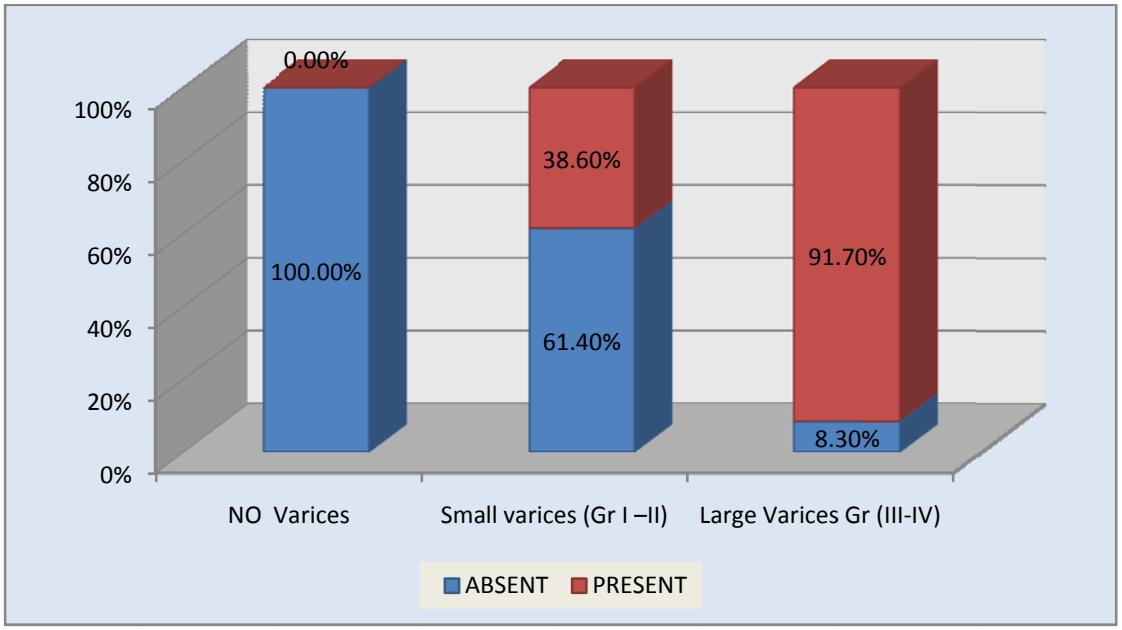
| SEX | FREQUENCY | PERCENT |
|---|---|---|
| MALE | 101 | 95.3 |
| FEMALE | 5 | 4.7 |
| TOTAL | 106 | 100 |



## ***CLINICAL FEATURES ANALYSIS***

**PALLOR**

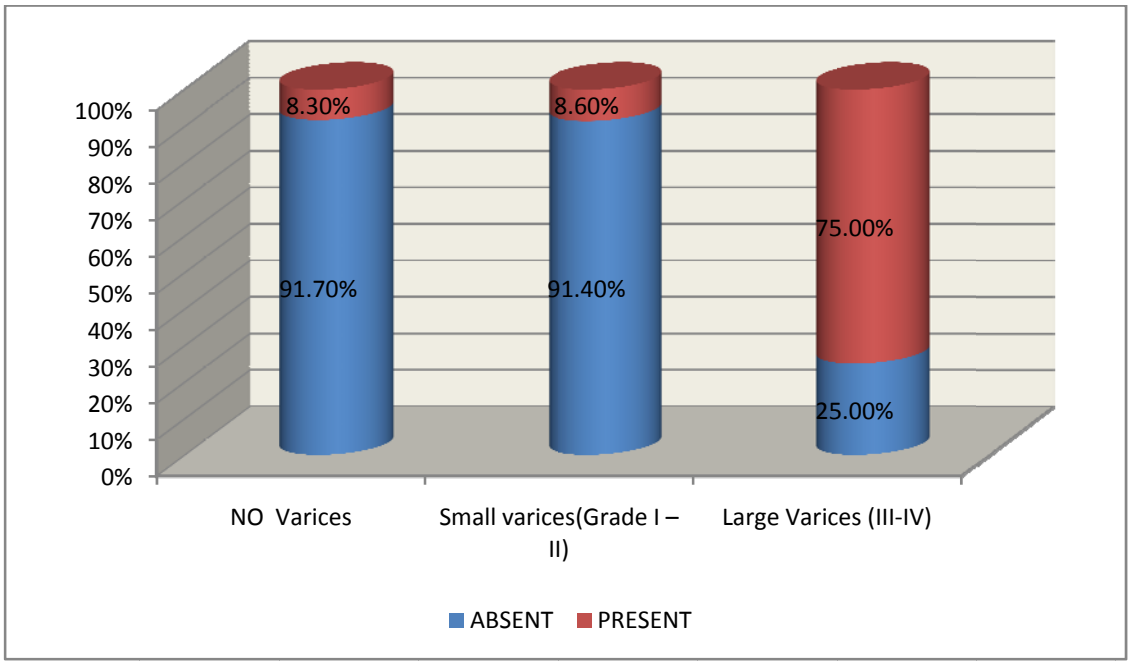
| Table 5 | | | Esophageal Varices | | | Total |
|---|---|---|---|---|---|---|
| | | | NO Varices | Small varices (Grade I –II) | Large Varices (III-IV) | |
| Pallor | Absent | Count | 12 | 43 | 2 | 57 |
| | | Percent | 100.0% | 61.4% | 8.3% | 53.8% |
| | Present | Count | 0 | 27 | 22 | 49 |
| | | Percent | 0.0% | 38.6% | 91.7% | 46.2% |
| Total | | Count | 12 | 70 | 24 | 106 |
| | | Percent | 100.0% | 100.0% | 100.0% | 100.0% |




In the study population,38.6% of patients with small varices and 91.7% of the patients with large varices had pallor implying the presence of pallor in patients with large varices

## ICTERUS

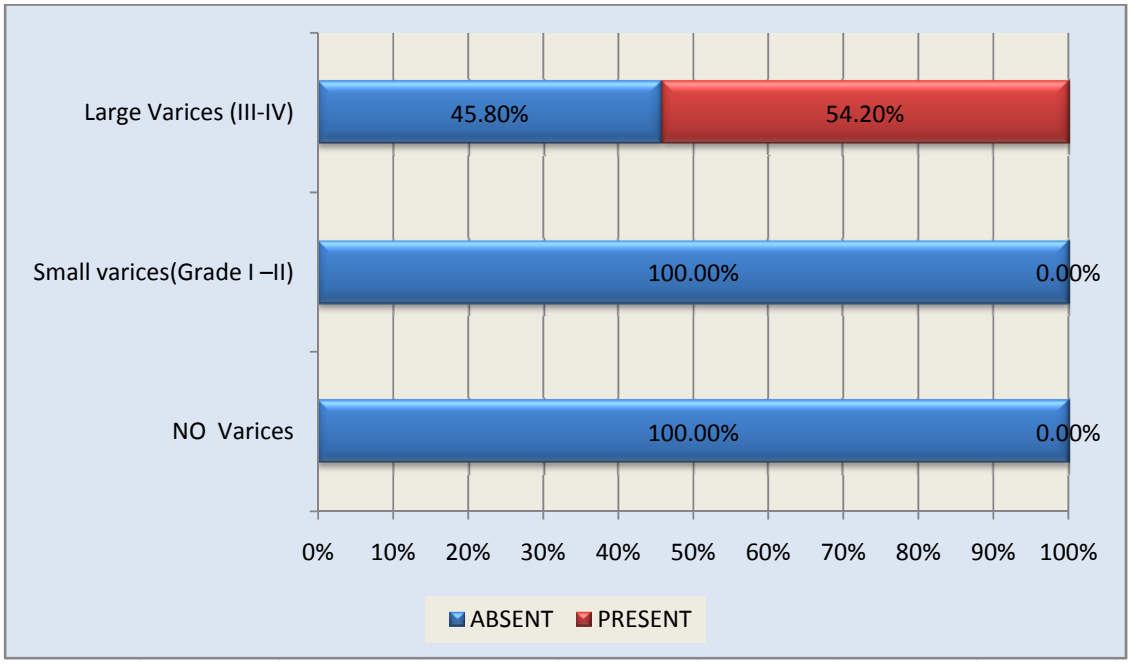
| Table 6 ICTERUS | | | ESOPHAGEAL VARICES | | | Total |
|---|---|---|---|---|---|---|
| | | | NO Varices | Small varices (Gr I –II) | Large Varices (Gr III-IV) | |
| | Absent | Count | 11 | 64 | 6 | 81 |
| | | Percent | 91.7% | 91.4% | 25.0% | 76.4% |
| | Present | Count | 1 | 6 | 18 | 25 |
| | | Percent | 8.3% | 8.6% | 75.0% | 23.6% |
| Total | | Count | 12 | 70 | 24 | 106 |
| | | Percent | 100.0% | 100.0% | 100.0% | 100.0% |




In the study,in patients with small varices 8.60% had icterus while in the large varices group the incidence was 75% implying presence of icterus in patients with larger varices group.

## SPIDER NAEVI

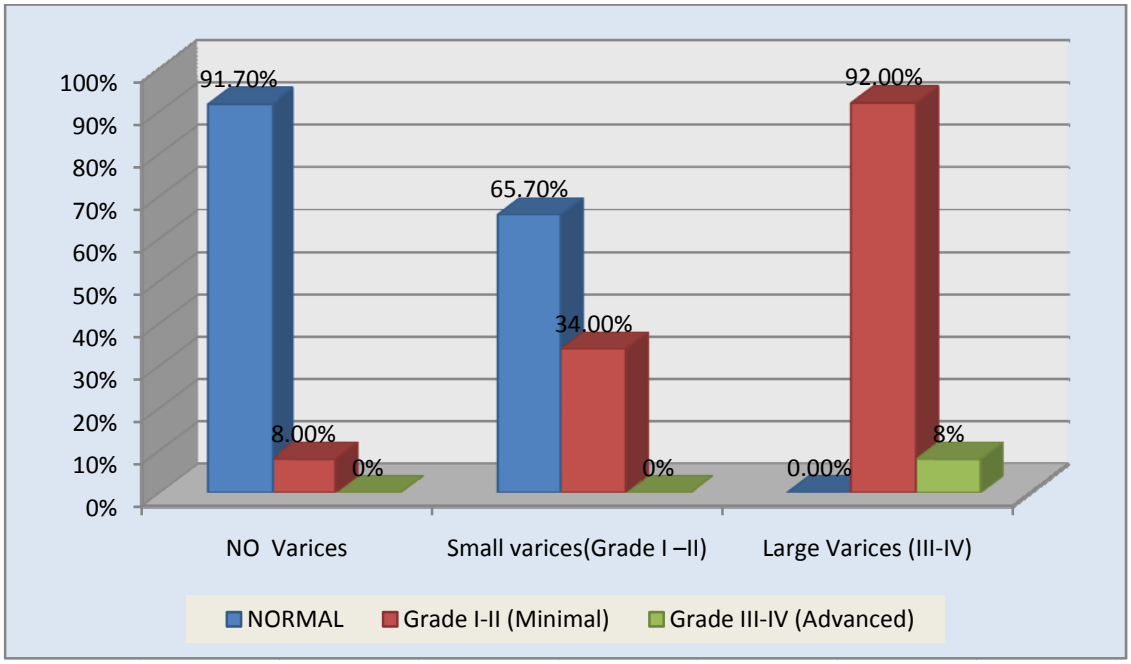
| Table 7 | | | ESOPHAGEAL VARICES | | | Total |
|---|---|---|---|---|---|---|
| | | | NO Varices | Small varices (Gr I –II) | Large Varices (Gr III-IV) | |
| Spider Naevi | ABSENT | Count | 12 | 70 | 11 | 93 |
| | | Percent | 100.0% | 100.0% | 45.8% | 87.7% |
| | PRESENT | Count | 0 | 0 | 13 | 13 |
| | | Percent | 0.0% | 0.0% | 54.2% | 12.3% |
| Total | | Count | 12 | 70 | 24 | 106 |
| | | | 100.0% | 100.0% | 100.0% | 100.0% |




In the study,spider naeviwas seen in 54.2% of the patients with large varices.

## HEPATIC ENCEPHALOPATHY

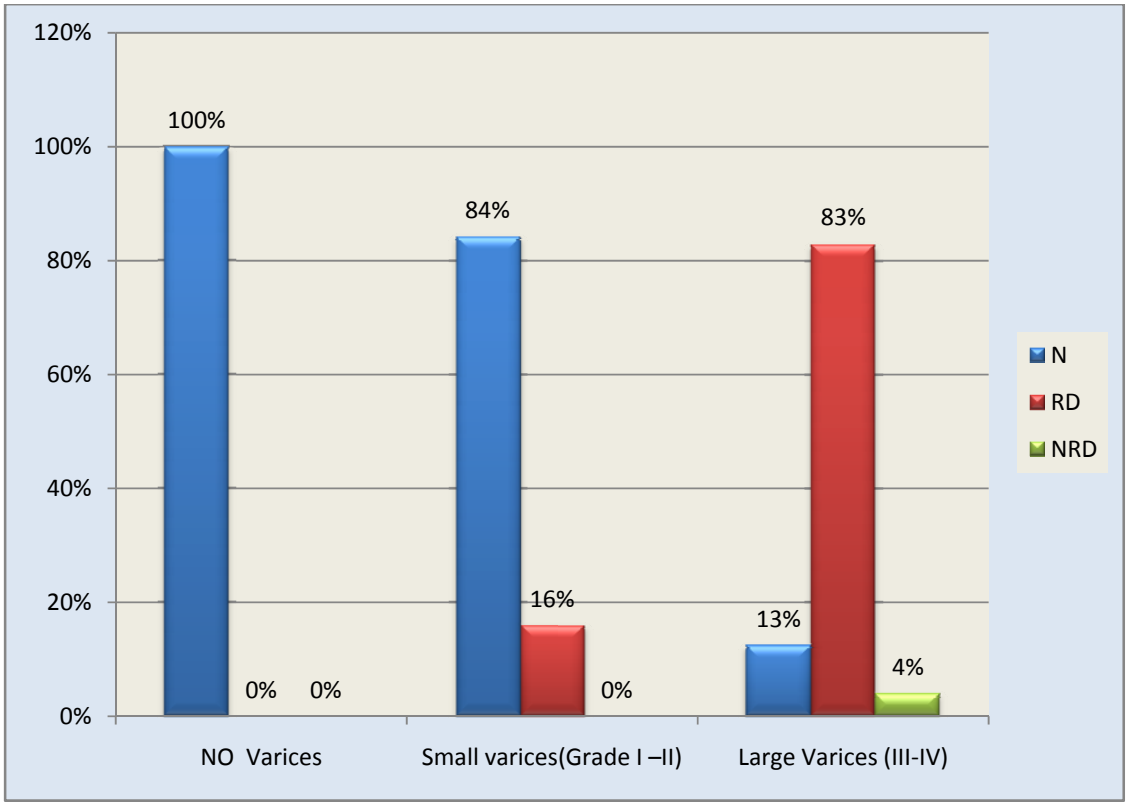
| Table 8 | | | ESOPHAGEAL VARICES | | | Total |
|---|---|---|---|---|---|---|
| | | | NO Varices | Small varices (Gr I – II) | Large Varices (Gr III-IV) | |
| Hepatic Encephalopathy | NORMAL | Count | 11 | 46 | 0 | 57 |
| | | Percent | 91.7% | 65.7% | 0.0% | 53.8% |
| | Gr I-II (Minimal) | Count | 1 | 24 | 22 | 47 |
| | | Percent | 8.3% | 34.3% | 91.7% | 44.3% |
| | Gr III-IV (Advanced) | Count | 0 | 0 | 2 | 2 |
| | | Percent | 0.0% | 0.0% | 8.3% | 1.9% |
| Total | | Count | 12 | 70 | 24 | 106 |
| | | Percent | 100.0% | 100.0% | 100.0% | 100.0% |



Our study demonstrates that hepatic encephalopathy was seen in 8%of the individuals with no varices,34% of the patients with small varices and 92% of the patients with large varices implying the increased incidence of hepatic encephalopathy at higher grades of varices.

## ASCITIS

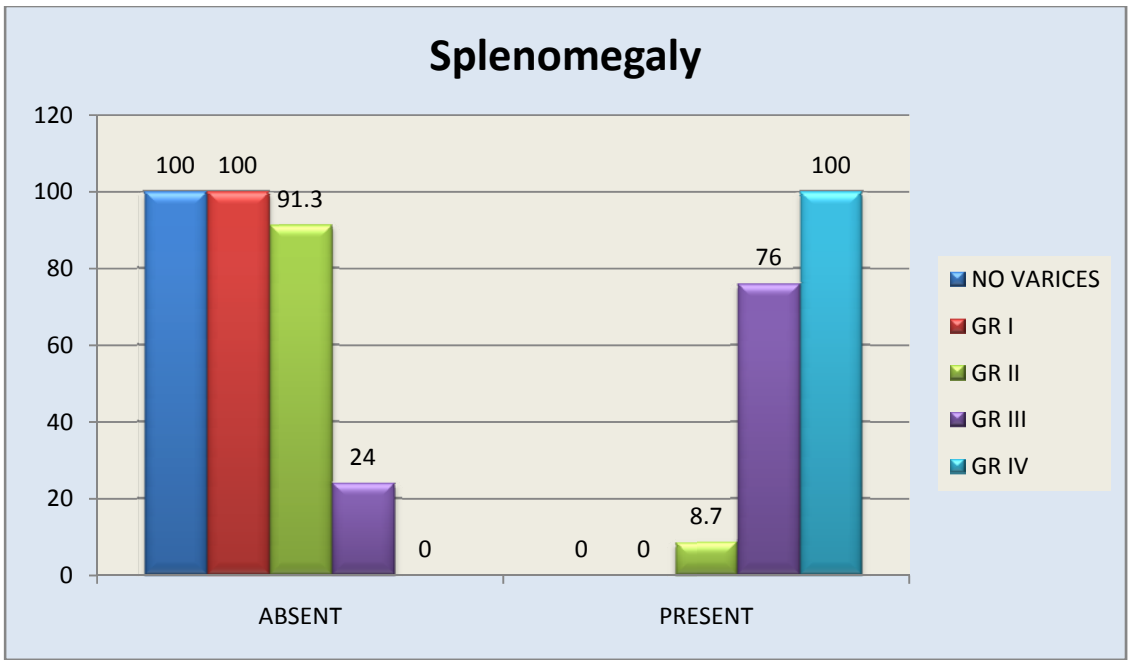
| Table 9 ASCITIS | | | ESOPHAGEAL VARICES | | | Total |
|---|---|---|---|---|---|---|
| | | | NO Varices | Small varices (Gr I –II) | Large Varices (Gr III-IV) | |
| | N | Count | 12 | 59 | 3 | 74 |
| | | Percent | 100.0% | 84.3% | 12.5% | 69.8% |
| | RD | Count | 0 | 11 | 20 | 31 |
| | | Percent | 0.0% | 15.7% | 83.3% | 29.2% |
| | NRD | Count | 0 | 0 | 1 | 31 |
| | | Percent | 0.0% | 0.0% | 4.2% | 29.2% |
| Total | | Count | 12 | 70 | 24 | 106 |
| | | Percent | 100.0% | 100.0% | 100.0% | 100.0% |




In the study,16% of the patients with small varices had ascites while in patients with large varices 83% had ascites responsive to diuretic while 4% had ascites that is resistant to diuretic.

## SPLENOMEGALY

| Table 10 | | No varices | I | II | III | IV |
|---|---|---|---|---|---|---|
| SPLENO-MEGALY | ABSENT | 12 | 24 | 42 | 4 | 0 |
| | Percent | 100% | 100% | 91.3% | 23.5% | 0% |
| | PRESENT | 0 | 0 | 4 | 13 | 7 |
| | Percent | 0% | 0% | 8.7% | 76.5% | 100% |
| | Total | 12 | 24 | 46 | 17 | 7 |
| | Percent | 100% | 100% | 100% | 100% | 100% |

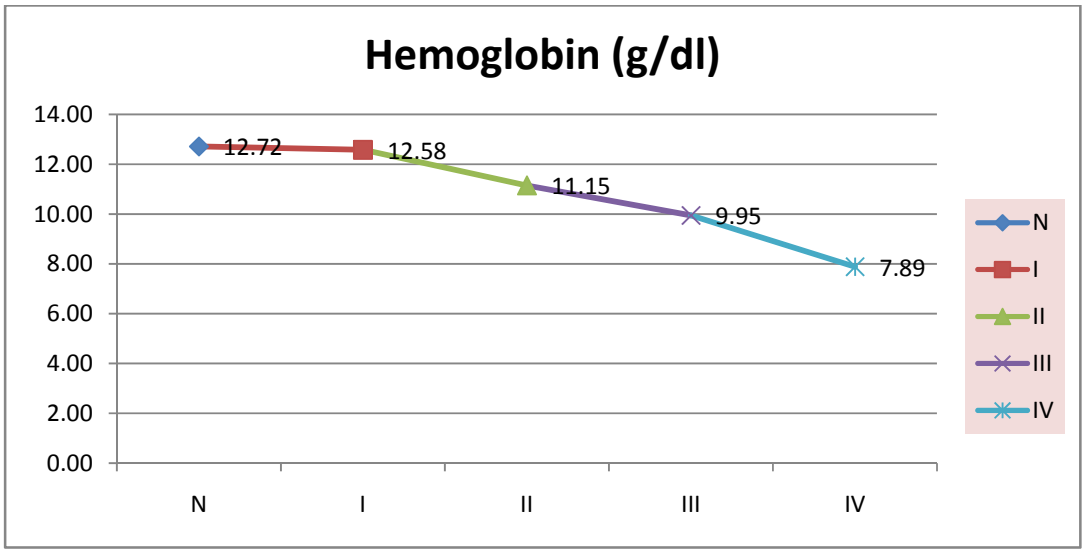



The study on the splenomegaly with the presence of varices showed 8.65% of the patients with smallvarices had splenomegaly while 76% of the patients with grade IIIvarices had splenomegaly while all the patients with grade IVvarices had splenomegaly implying the presence of splenomegaly in higher grades of varices.

## LABORATORY INVESTIGATIONS

## HEMOGLOBIN

| Table 11 | | N | MEAN | STD. DEVIATION |
|---|---|---|---|---|
| HEMOGLOBIN (g/dl) | NO | 12 | 12.7167 | 0.81779 |
| | I | 24 | 12.5833 | 1.10755 |
| | II | 46 | 11.15 | 1.38848 |
| | III | 17 | 9.9471 | 1.53953 |
| | IV | 7 | 7.8857 | 1.43228 |
| | TOTAL | 106 | 11.2434 | 1.82465 |

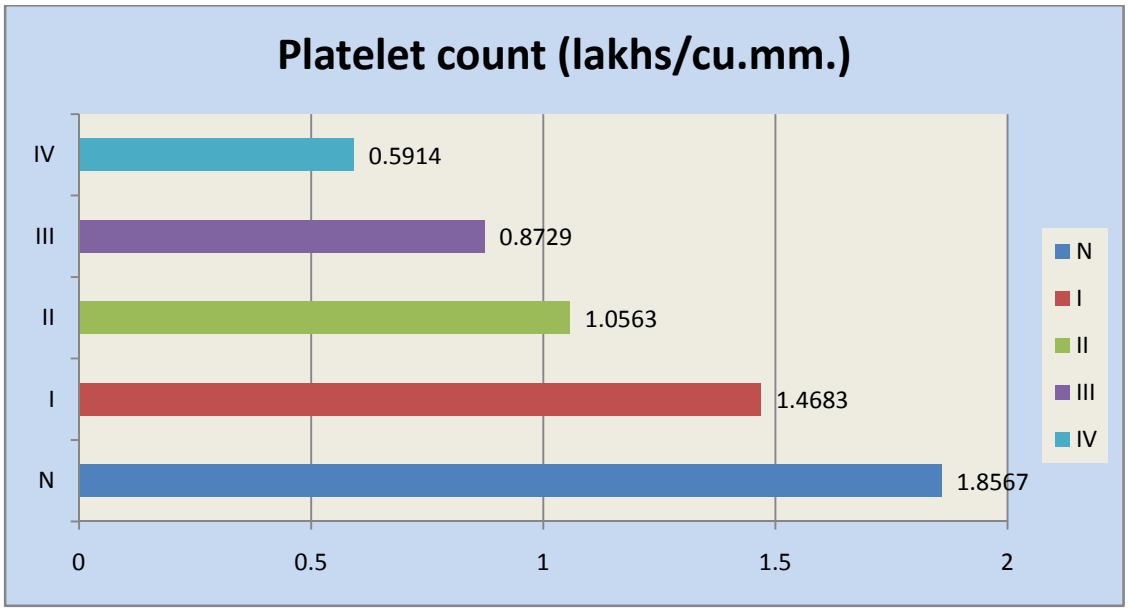



In the study population,57 had no pallor(53.8%) and 49 had pallor(46.2%).comparing the presence of pallor to the presence of varices 38.6% of patients with small varices (Grade I - II) had pallor and 91.70% of the patients with large varices (Grade III - IV) had pallor. From the study, it is seen that patients with higher degree of varices had pallor

## PLATELET COUNT

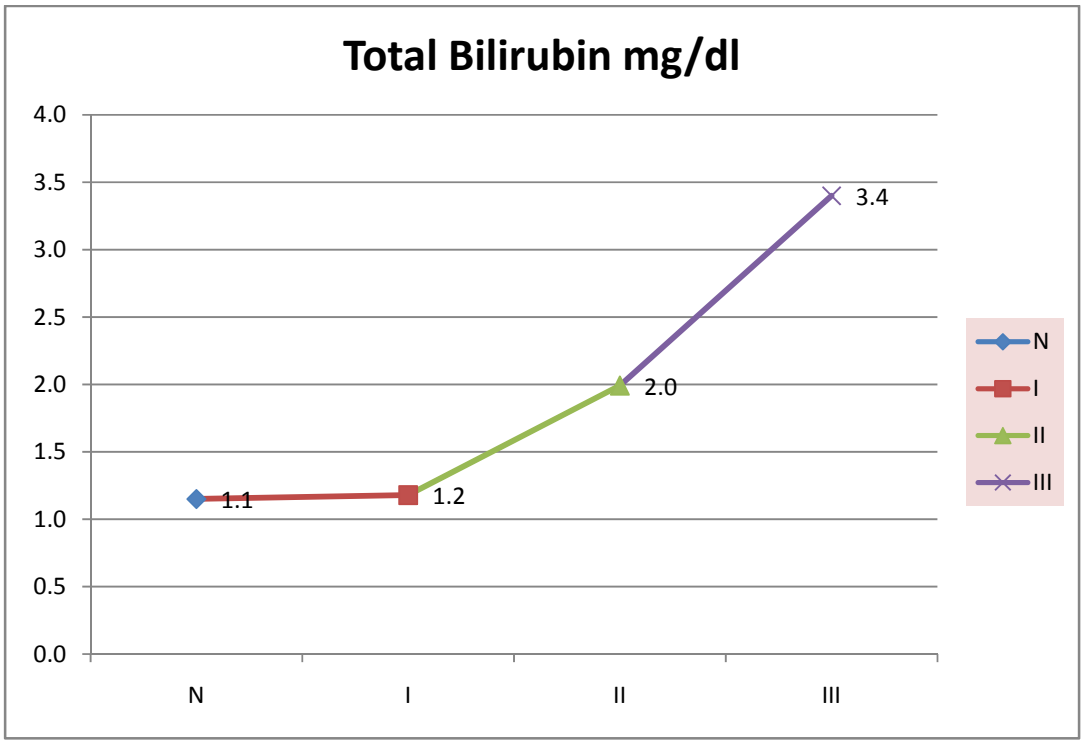
| Table 12 | | N | MEAN | STD. DEVIATION |
|---|---|---|---|---|
| PLATELET COUNT (LAKHS/CU.MM.) | N | 12 | 1.8567 | 0.60331 |
| | I | 24 | 1.1683 | 0.48668 |
| | II | 46 | 1.0563 | 0.26619 |
| | III | 17 | 0.8729 | 0.15608 |
| | IV | 7 | 0.5914 | 0.07819 |
| | TOTAL | 106 | 1.1801 | 0.49075 |

In our study,mean platelet count in No varices group(1.8 L/cu.mm.), grade I (1.16L/cu.mm.), grade II (1.05 L/cu.mm.),grade III (0.87 L/cu.mm.), grade IV ( 0.59 L/cu.mm.) with a significant p value of <0.001 signifying thrombocytopenia as a marker for esophageal varices and its severity.



## TOTAL BILIRUBIN

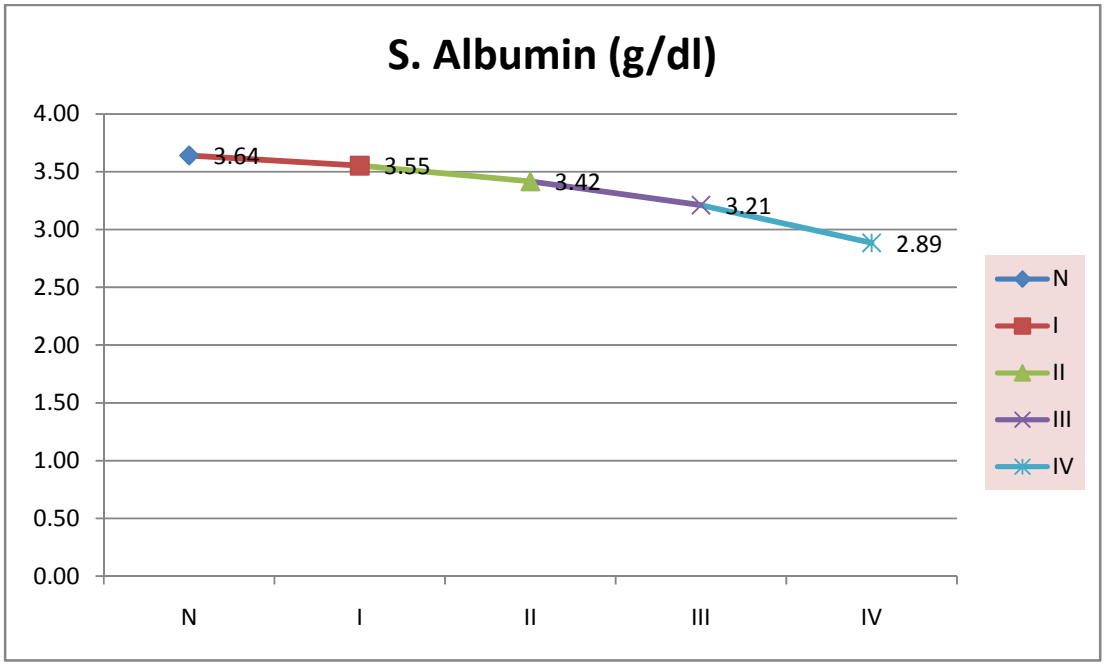
| Table 13 | | N | MEAN | STD. DEVIATION |
|---|---|---|---|---|
| TOTAL BILIRUBIN (mg/dl) | N | 12 | 1.15 | 0.70903 |
| | I | 24 | 1.1792 | 0.52584 |
| | II | 46 | 1.9913 | 0.57497 |
| | III | 17 | 3.4 | 1.96977 |
| | IV | 7 | 4.5143 | 2.34693 |
| | TOTAL | 106 | 2.1047 | 1.45781 |




Patients with higher grades of variceshad higher values of serum bilirubin.

## S. ALBUMIN

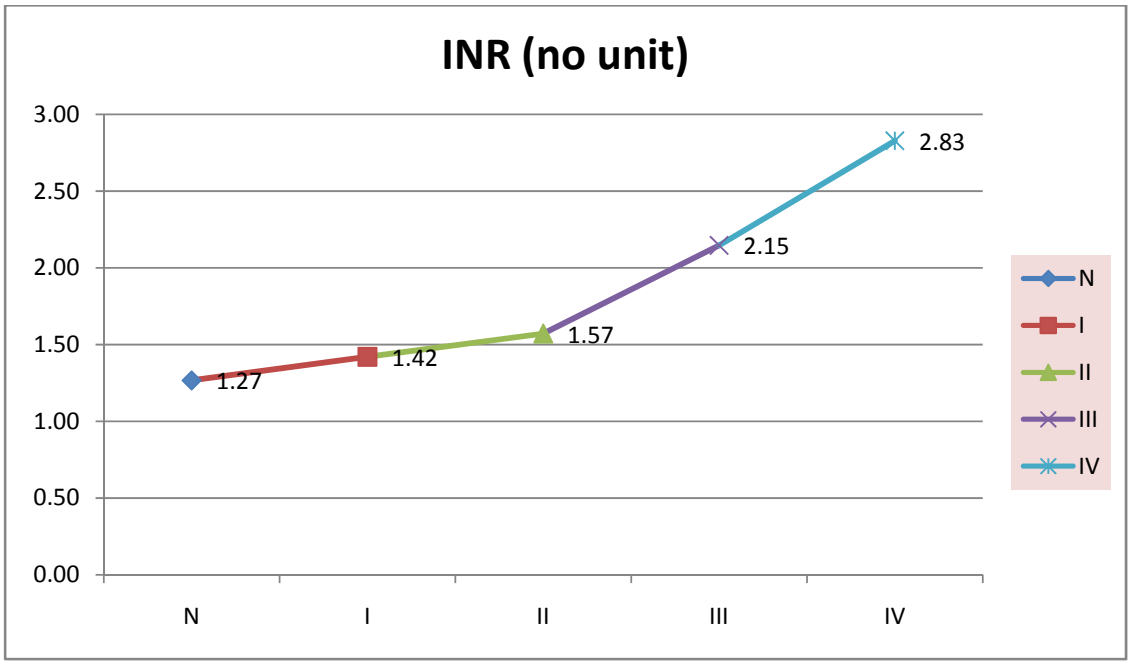
| Table 14 | | N | MEAN | STD. DEVIATION |
|---|---|---|---|---|
| S. ALBUMIN g/dl | N | 12 | 3.6417 | 0.1379 |
| | I | 24 | 3.5542 | 0.15874 |
| | II | 46 | 3.4174 | 0.21008 |
| | III | 17 | 3.2118 | 0.39032 |
| | IV | 7 | 2.8857 | 0.38483 |
| | Total | 106 | 3.4057 | 0.30608 |




Patient with no varices group had a mean albumin of 3.64 g/dL, grade I (3.55 g/dL), grade II (3.42 g/d L), grade III (3.21 g/dl), and grade IV (2.89 g/dl) indicating presence of hypoalbunminemia in higher grades of varices.

**INR**

| Table 15 | | N | MEAN | STD. DEVIATION |
|---|---|---|---|---|
| INR (no unit) | N | 12 | 1.2667 | 0.25346 |
| | I | 24 | 1.4208 | 0.29924 |
| | II | 46 | 1.5717 | 0.28803 |
| | III | 17 | 2.1471 | 0.82395 |
| | IV | 7 | 2.8286 | 0.99785 |
| | Total | 106 | 1.6783 | 0.62091 |

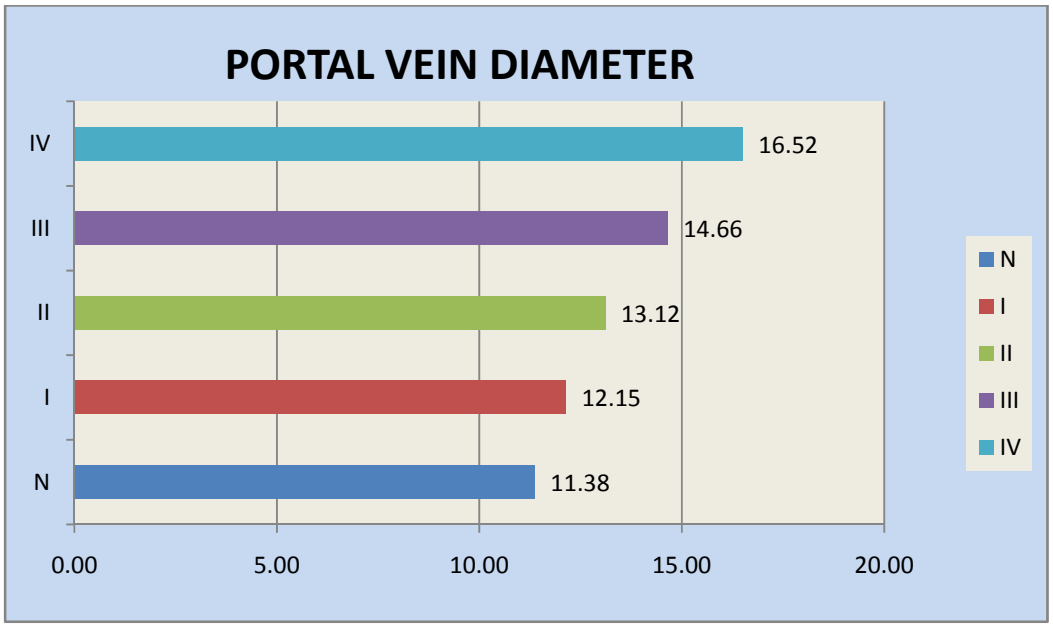



Patients with higher grades of varices had prolongation of INR implying clotting factor abnormality in patients with higher varices group.

## ULTRASONOGRAM FINDINGS

| Table 16 | | N | MEAN | STD. DEVIATION |
|---|---|---|---|---|
| PORTAL VEIN DIAMETER (in mm) | N | 12 | 11.3833 | 1.02144 |
| | I | 24 | 12.1542 | 0.81773 |
| | II | 46 | 13.1261 | 0.94197 |
| | III | 17 | 14.6647 | 1.49246 |
| | IV | 7 | 16.5286 | 2.25663 |
| | TOTAL | 106 | 13.1802 | 1.72673 |

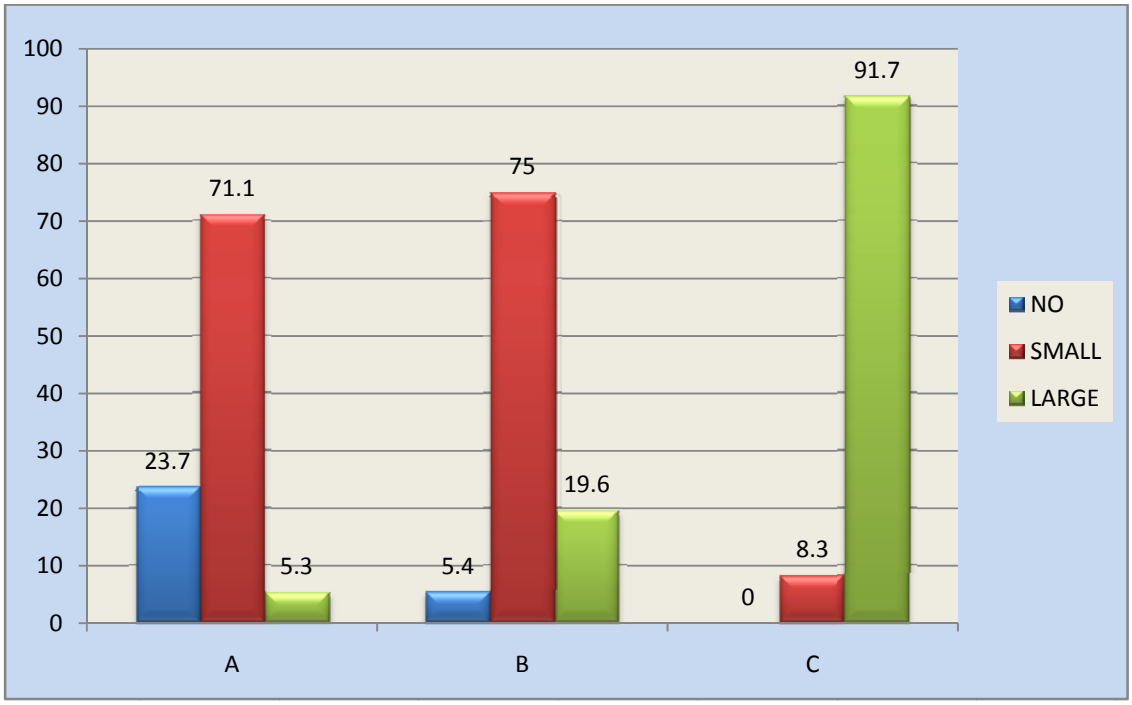
The relationship of portal vein diameter to the presence of varices shows mean PVD in the No varices group (11.38), gr I(12.15), gr II(13.12), gr III (14.66), gr IV ( 16.53) with a significant p value of < 0.001 implying a significant corelationship of portal venous diameter to the presence of varices and its severity.



## CHILD PUGH SCORE

| CHILD PUGH SCORE VS ESOPHAGEAL VARICES | | | | | | |
|---|---|---|---|---|---|---|
| **Table 17** | | | ESOPHAGEAL VARICES | | | TOTAL |
| | | | NO VARICES | SMALL VARICES (GR I –II) | LARGE VARICES (GR III-IV) | |
| **CHILD PUGH SCORE** | A | COUNT | 9 | 27 | 2 | 38 |
| | | PERCEMT | 23.7% | 71.1% | 5.3% | 100.0% |
| | B | COUNT | 3 | 42 | 11 | 56 |
| | | PERCENT | 5.4% | 75.0% | 19.6% | 100.0% |
| | C | COUNT | 0 | 1 | 11 | 12 |
| | | PERCENT | 0.0% | 8.3% | 91.7% | 100.0% |
| **TOTAL** | | COUNT | 12 | 70 | 24 | 106 |
| | | PERCENT | 11.3% | 66.0% | 22.6% | 100.0% |

38 out of 106 were in Class A (35.8%). Of which 23.7% had no varices, 71.1% had small varices and 5.3% of patients had large varices.56 out of 106 were in Child Pugh Class B (52.8%), of which 5.4% had no varices, 75% had small varices and 19.6% had large varices.12 out of 106 were in Child Pugh Class C (11.3%), of which 91.7% had large varices, while small varices were found in 8.3% of the individuals indicating the presence of varices and its severity to Child Pugh score.


100
90
80
70
60
50
40
30
20
10
0
23.7
71.1
5.3
5.4
75
19.6
0
8.3
91.7
A
B
C
NO
SMALL
LARGE

# 6. DISCUSSION

Our study was conducted in patients with alcoholic liver disease with cirrhosis of liver to study the Child-Pugh score as a non-endoscopic predictor for the presence of esophageal varices and its role in assessing the variceal severity in the prediction of esophageal varices. Our study population included 106 patients admitted with liver disease diagnosed either by clinical, laboratory or sonographical methods. In all patients under study detailed history was taken, basic laboratory investigations and ultrasound was done. Patients are then undertaken for endoscopy to screen for varices after ruling out other causes for cirrhosis.Analysis was then made to correlate between the Child-Pugh score of the patients with the degree and severity of the esophageal varices using chi square test (ANOVA). Our study also included other parameters that are indicators for varices in patients with alcoholic cirrhosis.Following were the observation made from our study.

**Age distribution:** Out of the 106 patients majority were in the age group of 41-65 years (54.7%), with a mean age group of 43.2 years and belongs to the Child Pugh score B(52.8%).In our study 88.7% had varices and 11.3% had

no varices. In the study, majority of the patients with varices fall in the middle age group comparable to the previous study, Arul Prakash sarangapani, Chitra Shanmugham*et al*[57].

**Sex distribution:** In our study 101 out of 106 were males(95.3%) and 5 were females(4.7%).

**Clinical Findings:**In the study evaluation of the clinical signs out of the 106 patients 57 had no pallor(53.8%) and 49 had pallor(46.2%).comparing the presence of pallor to the presence of varices 38.6% of patients with small varices (Grade I - II) had pallor and 91.70% of the patients with large varices (Grade III - IV) had pallor. From the study,it is seen that patients with higher degree of varices had pallor comparable to the earlier study, Arul Prakash Sarangapani, ChitraShanmugham,et al[57].

Icterus was absent in 81 of the patients(76.4%) and present in 25 of the patients(23.6%).In patients with small varices, icterus was present in 8.60% of the individuals while in large varices75% had icterus. From the study the presence of icterus correlates with a higher degree of varices.

Spider naevi as a clinical sign was present in 13 patients(12.3%). With a incidence of 54.20% in patients with large varices. So from the study the

presence of spider nevi indicates severity of varices in patients with alcoholic cirrhosis.

On the comparison of the presence of hepatic encephalopathy with the esophageal varices in the study,49 patients were in the different grades of hepatic encephalopathy (46.2%). Of which majority of the individuals (44.3%) were in grade I-II and 1.9% of the patients were in grade III - IV hepatic encephalopathy.43.4% of the patients with small varices had grade I-II hepatic encephalopathy compared to 91.7% of the patients with large varices.8.3% of the patients with large varices were in advanced (grade III - IV) stages of hepatic encephalopathy proving that presence of hepatic encephalopathy correlates with higher degree of varices.

On comparing the grading of ascitis with the severity of varices, out of the 106,69.8% had no ascitis and 30.1% had ascitis. In patients with small varices 84.3% had no ascitis while 15.7% had ascitis responsive to diuretics. In patients with large varices,12.5%were normal while 83.3% had ascitis responsive to diuretics and 4.2% had ascitis that was resistant to diuretic. From the study, ascitis is not a reliable marker for varices but the presence higher grades of ascitis indicates larger varices in patients with alcoholic cirrhosis.

In the study, splenomegaly was seen in 23% of the individuals while 77% had no splenomegaly. In patients with grade II varices ,8.7% had splenomegaly, and in grade III 76% had splenomegaly while it is a constant finding in patients with grade iv varices group implying the presence of splenomegaly correlates with the presence of larger varices in patients with alcoholic cirrhosis.The results are comparable to the national study,Arul Prakash Sarangapani, ChitraShanmugham,*et al*[57].

**Laboratory Parameters:** The mean Hemoglobin level in No varices group – 12.72 g/dl, Grade I varices – 12.58 g/dl, Grade II varices – 11.15g/dl, Grade III varices – 9.95 g/dl and Grade IV varices – 7.89 g/dl indicating patients with higher grades of varices have predominantly lower Hemoglobin.

The mean levels of Serum albumin in No varices – 3.64 g/dl, Grade I varices group – 3.55 g/dl, Grade II varices – 3.42 g/dl, Grade III varices – 3.21 g/dl and Grade IV – 2.89 g/dl implying hypoalbuminemia in higher grades of Esophageal varices.

The mean INR in No varices – 1.27, Grade I varices group – 1.42 Grade II varices – 1.57, Grade III varices – 2.15 and Grade IV – 2.83 with increased incidence of clotting factor abnormality with higher grades of

Esophageal varices. The values are comparable to the previous study, D.LaBreque, A.G.Khan, S.K.Sarin*et al*[58].

The mean Platelet counts in No varices group – 1.8 lakh/cumm, Grade I varices group – 1.16 lakh/cumm, Grade II varices – 1.05 lakh/cumm, Grade III varices – 0.87 lakh/cumm and Grade IV – 0.59 lakh/cumm with significant p value of < 0.001. From the study, presence of thrombocytopenia is a marker for the presence of esophageal varices and also indicates the severity of varices comparable to the study, Arul Prakash sarangapani, ChitraShanmugham,*et al*[57]. D.La Breque, A.G.Khan, S.K.Sarin*et al*[58].

**Ultra Sonography:** USG findings in patients with alcoholic liver disease where the portal vein diameter is assessed, the mean values were No varices group – 11.38 mm, Grade I varices group – 12.95 mm, Grade II varices – 13.12 mm, Grade III varices – 14.66 mm and Grade IV – 16.52 mm with significant p value of < 0.001. So our study proves that portal vein diameter can be used to predict the presence of esophageal varices and its severity in patient with alcoholic cirrhosis comparable to the earlier study, D. La Breque, A.G.Khan, S.K.Sarin*et al*[58].

**Child Pugh Score Assessment:**Comparing the Child Pugh Score with the Esophageal Varices shows 38 out of 106 were in Class A (35.8%). Of which 23.7% had no varices, 71.1% had small varices and 5.3% of patients had large varices.

56 out of 106 were in Child Pugh Class B (52.8%), of which 5.4% had no varices, 75% had small varices and 19.6% had large varices.

12 out of 106 were in Child Pugh Class C (11.3%), of which 91.7% had large varices, while small varices were found in 8.3% of the individuals.

The study concludes that Child Pugh Score can be used as an effective predictor for varices and the severity of the varices as comparable to the earlier study, Arul Prakash Sarangapani, ChitraShanmugham,*et al*[57], D.La Breque, A.G.Khan, S.K.Sarin*et al*[58].

# 7. SUMMARY

The following results were obtained from our study:

- Majority of the patients with alcoholic cirrhosis belongs to the middle age group and falls under Child Pugh score B.
- In our study, alcoholic cirrhosis of liver was more common in males when compared to females.This age difference can be due to lower incidence of alcohol in females in South India.
- Majority of the patients with large varices had pallor, icterus,spider naevi and splenomegalysignifying that the above parameters can be taken as markers for the presence of large varices in patients with alcoholic cirrhosis.
- Most of the patients with varices had hepatic encephalopathy of which majority falls under grade I-II.Advanced stages of hepatic encephalopathy are seen in patients with large varices.
- Ascitis was commonly seen in patients with large varices and most of the cases were responsive to diuretics while a small percentage of cases in the large varices group were diuretic resistant.
- Patients with higher degree of varices had low hemoglobin, hypoalbuminemia and prolongation of INR.

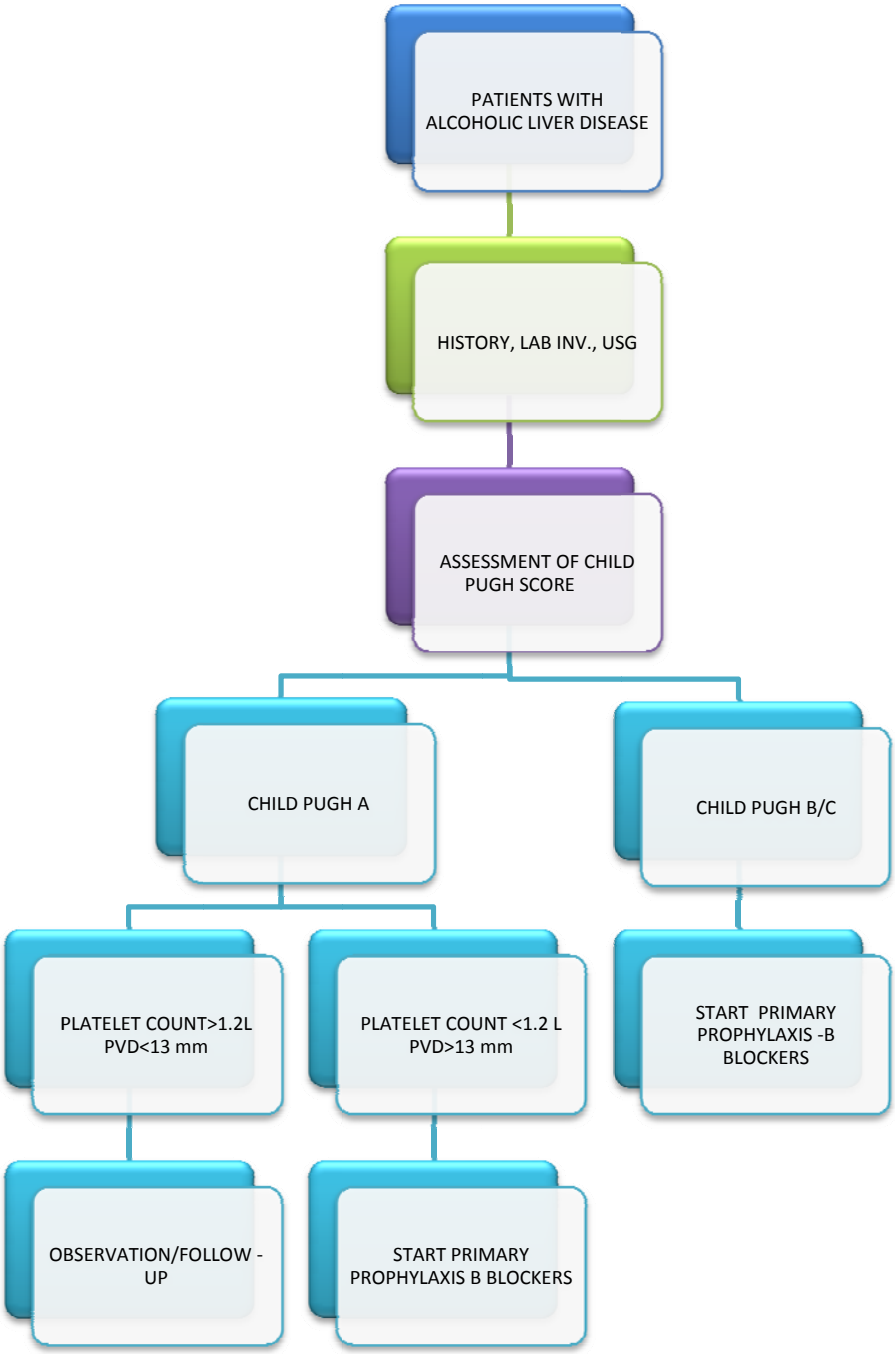
- In the study, analysis on the platelet count had a significant p value implying Thrombocytopenia as an indicator for the presence of esophageal varices and also correlates with its severity in patients with alcoholic cirrhosis.
- Ultrasound assessment of portal venous diameter in the study population showed a significant p value correlating its association with the presence of esophageal varices.
- Child Pughs score had a significant p value and showed the significance of the comparison of the score with the presence of esophageal varices and its severity. Majority of the patients fall under Child Pugh Score B.Patients with higher score had higher grades of varices. In our study, a significant proportion of patients falling under Child Pugh score A also had varices signifying the need for primary prophylaxis at the initial stages.

# 8. CONCLUSION

Alcoholic liver disease is on an alarming rising trend worldwide.Variceal bleed carries a significant morbidity and mortality in patients with alcoholic liver disease. Hence, early detection of varices is of prime importance. But to detect varices currently we rely upon endoscopy and it remains the only cornerstone which has added disadvantages of reduced availability,less patient compliance,increased risk of complications and its mortality,delay in the treatment and increased health care costs.To alleviate these factors especially in a peripheral setup with reduced accessibility for endoscopic services,use of other non-invasive parameters will be helpful to overcome the need.So, in the search for different non endoscopic parameters that can be relied upon,the present study shows a significant correlation of Child Pugh score with the presence of esophageal varices and also correlates with the severity of the varices. Other parameters like the platelet count, portal vein diameter also had a significant association with the presence of esophageal varices. The study shows majority of the patients with Child Pugh score B and C had varices while in our study, Child Pugh score A also had a significant proportion of varices(76.4%) imposing the search for varices from the grassroot level and the need for timely intervention.

The limitation of the study is that it involves a smaller population compared to the disease burden and results are based on the study conducted in a single institute.The study also had inter-observer variation on the endoscopy findings. So it is recommended to conduct the study in large,multicentric trials to verify the result.

From the study, an algorithm approach to a patient with alcoholic cirrhosis is as follows comparable to earlier study[58].



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# 10. ANNEXURES

## ANNEXURE – I

**"A STUDY ON CHILD PUGH SCORE AS A NON ENDOSCOPIC PREDICTOR FOR ESOPHAGEAL VARICES IN PATIENTS WITH ALCOHOLIC DISEASE"**

**QUESTIONAIRE**

**PATIENT DETAILS:**

Name: Age: Sex:

IP No. :

**ON ADMISSION:**

Main Complaints :

H/o jaundice

H/o abdominal distension

H/O abdominal pain

H/o pedal oedema

H/o reduced urine output,

H/O constipation,diarrhoea

H/o breathlessness

H/o orthopnoea/paroxysmal nocturnal dyspnea

H/o haemetemesis

H/o melena

H/o  seizures

H/o altered sensorium

H/o altered sleep pattern

H/o chest pain

H/o fever

H/o cough,sputum

H/o intake of any drugs

H/o recent blood transfusions or injections.

Co – Morbid Illness :

Significant Past History :

**CLINICAL EXAMINATION:**

Pulse : BP :

RR : Temp:

**GENERAL EXAMINATION:**

Pallor,

Icterus,

Cyanosis,

Clubbing,

Generalized lymyphadenopathy,

Pedal or presacral edema.

Signs of liver cell failure:

Parotidomegaly, Leuconychia, Gynaecomastia, Duputyrens contracture, Palmar erythema, Spidernaevi, testicular atrophy.

**SYSTEMIC EXAMINATION:**

Cardiovascular System:

Respiratory System:

Abdominal Examination:

Central Nervous System:

**INVESTIGATIONS :**

**Complete Hemogram**

Hemoglobin:

Total Count/ Differential Count:

Platelet Count:

Hematocrit:

**Complete Liver Function Test**

Total Bilirubin:

Direct/Indirect Bilirubin:

SGOT/SGPT:

Serum ALP:

Total Protein:

Serum Albumin:

Albumin/Globulin ratio:

**Prothrombin Time/INR:**

Bleeding time/Clotting time:

Blood Grouping & Rh typing:

**Viral Markers:**

**Upper Gastro Intestinal Endoscopy:**

**Child Pugh Score:**

# ANNEXURE – II

## AUDIT QUESTIONNAIRE

| Question | 0 | 1 | 2 | 3 | 4 |
|---|---|---|---|---|---|
| 1. How often do you have a drink containing alcohol? | Never | Monthly or less | 2–4 Times a month | 2–3 Times a week | 4 Or more times a week |
| 2. How many drinks containing alcohol do you have on a typical day when you are drinking? | 1 or 2 | 3 or 4 | 5 or 6 | 7–9 | 10 or more |
| 3. How often do you have 5 or more drinks on one occasion? | Never | Less than monthly | Monthly | Weekly | Daily or almost daily |
| 4. How often during the last year have you found that you were not able to stop drinking once you had started? | Never | Less than monthly | Monthly | Weekly | Daily or almost daily |
| 5. How often during the last year have you failed to do what was normally expected of you because of drinking? | Never | Less than monthly | Monthly | Weekly | Daily or almost daily |
| 6. How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session? | Never | Less than monthly | Monthly | Weekly | Daily or almost daily |
| 7. How often during the last year have you had a feeling of guilt or remorse after drinking? | Never | Less than monthly | Monthly | Weekly | Daily or almost daily |
| 8. How often during the last year have you been unable to remember what happened the night before because of your drinking? | Never | Less than monthly | Monthly | Weekly | Daily or almost daily |
| 9. Have you or someone else been injured because of your drinking? | No | | Yes, but not in the last year | | Yes, during the last year |
| 10. Has a relative, friend, doctor, or other health-care worker been concerned about your drinking or suggested you cut down? | No | | Yes, but not in the last year | | Yes, during the last year |

AUDIT, Alcohol Use Disorders Identification Test.
To score the AUDIT questionnaire, sum the scores for each of the 10 questions. A total ≥8 for men up to age 60, or ≥4 for women, adolescents, or men over the age of 60 is considered to be a positive screening test.

# ANNEXURE – III

## PATIENT CONSENT FORM

| | | |
|---|---|---|
| Study Detail | : | **"A STUDY ON CHILD PUGH SCORE AS A NON-ENDOSCOPIC PREDICTOR OF OESOPHAGEAL VARICES IN PATIENTS WITH ALCOHOLIC LIVER DISEASE"** |
| Study Centre | : | Rajiv Gandhi Government General Hospital, Chennai. |
| Patient's Name | : | |
| Patient's Age | : | |
| In Patient Number | : | |

Patient may check (☑) these boxes

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction. ☐

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected. ☐

I understand that sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study. ☐

I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well being or any unexpected or unusual symptoms. ☐

I hereby consent to participate in this study ☐

I hereby give permission to undergo complete clinical examination and diagnostic tests including hematological, biochemical, radiological tests. ☐

Signature/thumb impression

Signature of Investigator

Patient's Name and Address:

Study Investigator's Name: **Dr. SINDHU.P**

## INFORMATION SHEET

We are conducting a study on

**"A STUDY ON CHILD PUGH SCORE AS A NON-ENDOSCOPIC PREDICTOR OF OESOPHAGEAL VARICES IN PATIENTS WITH ALCOHOLIC LIVER DISEASE"** among patients attending Rajiv Gandhi Government General Hospital, Chennai and for that your specimen may be valuable to us.

The purpose of this study is

1. To use Child Pugh Score as an alternative non invasive indicator for oesophageal varices in patients with alcoholic liver disease.

We are selecting certain cases and if you are found eligible, we may be using 8ml of blood sample to be collected; in EDTA for Complete hemogram, Complete Liver function test and Prothrombin time/INR will be taken. We also need to take an USG abdomen and perform UGI Endoscopy to assess varices.

The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled.

The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Signature of Investigator | Signature of Participant

Date :
Place :

# ANNEXURE – IV

# TAMIL CONSENT FORM

## ஆராய்ச்சி ஒப்புதல் படிவம்

ஆராய்ச்சியின் தலைப்பு:- **மது அருந்துவதால் கல்லீரலில் ஏற்படும் இழைநார் வளர்ச்சி நோயின் விளைவாகத் தோன்றும் இரத்த நாள வீக்கத்தை உள்நோக்கி குழாய் அல்லாமல் சைல்டு புக் (Child Pugh) அளவின் மூலம் கண்டறிதல் பற்றிய ஆய்வு.**

**பங்கு கொள்பவரின் பெயர்:-**

**ஆராய்ச்சி செய்பவரின் பெயர்:-** சிந்து பா

**ஆராய்ச்சி மையம்:-** ராஜிவ்காந்தி அரசு பொது மருத்துவமனை,
சென்னை - 600003.

எனும் நான் எனக்குக் கொடுத்துள்ள தகவல் தாளை படித்துப் புரிந்து கொண்டேன். நான் பதினெட்டு வயதைக் கடந்துள்ளதால், என் சுயநினைவுடனும் முழு சம்மதத்துடனும் இந்த ஆய்வில் என்னைச் சேர்த்துக் கொள்ளச் சம்மதிக்கிறேன்.

1. நான் எனக்களிக்கப்பட்ட ஒப்புதல் படிவத்தையும் தகவல்களையும் படித்து புரிந்து கொண்டேன்.
2. ஒப்புதல் படிவத்தில் உள்ள தகவல்கள் எனக்கு விளக்கிக் கூறப்பட்டன.
3. ஆய்வின் தன்மை எனக்கு விளக்கப்பட்டது.
4. என் உரிமைகளையும் பொறுப்புகளையும் ஆராய்ச்சியாளர் விளக்கிக் கூறினார்.
5. நான் இதுவரை எடுத்துள்ள / எடுத்துக் கொண்டிருக்கும் அனைத்து விதமான சிகிச்சை முறைகளையும் ஆராய்ச்சியாளரிடம் கூறியுள்ளேன்.
6. இந்த ஆராய்ச்சியால் ஏற்படும் தீமைகள் பற்றி விளக்கப்பட்டன.

**ஆய்வின் நடுவில் அதிலிருந்து விலகிக் கொள்ள நினைத்தால்:-**

இந்த ஆய்வில் பங்கேற்பது தங்களின் சொந்த விருப்பமே. மேலும் ஆய்வின் நடுவில் எந்த நேரத்திலும், எக்காரணமும் கூறாமல் விலகிக் கொள்ள தங்களுக்கு முழு உரிமையும் உண்டு. இருப்பினும் ஆயவிலிருந்து விலகுவதற்கு முன் ஆராய்ச்சிக்குழுவுடன் கலந்து ஆலோசிப்பது உகந்தது எனப் பரிந்துரைக்கப்படுகின்றது.

ஆராய்ச்சியாளர் கையொப்பம் பங்கேற்பவரின் கையொப்பம்

தேதி : தேதி :

**<u>ஆராய்ச்சியில் பங்கேற்பவர்க்கான தகவல் அறிக்கை</u>**

ஆராய்ச்சியின் தலைப்பு:- **மது அருந்துவதால் கல்லீரலில் ஏற்படும் இழைநார் வளர்ச்சி நோயின் விளைவாகத் தோன்றும் இரத்த நாள வீக்கத்தை உள்நோக்கி குழாய் அல்லாமல் சைல்டு புக் (Child Pugh) அளவின் மூலம் கண்டறிதல் பற்றிய ஆய்வு.**

**பங்கு கொள்பவரின் பெயர்:-**

**ஆராய்ச்சி செய்பவரின் பெயர்:-** சிந்து பா

**இடம்:-** ராஜிவ்காந்தி அரசு பொது மருத்துவமனை, சென்னை - 600003.

இந்த ஆராய்ச்சி / ஆய்வு / செய்முறை / சோதனையில் தாங்கள் பங்கேற்க அழைக்கிறோம். இந்த தகவல் அறிக்கையில் கூறப்பட்டிருக்கும் தகவல்கள் தாங்கள் இந்த ஆராய்ச்சியில் பங்கேற்கலாமா வேண்டாமா என்பதை முடிவு செய்ய உதவியாக இருக்கும். இந்தப் படிவத்தில் உள்ள தகவல்கள் பற்றி உங்கள் சந்தேகங்களை நீங்கள் தயங்காமல் கேட்கலாம்.

**இந்த ஆய்வின் நோக்கம் என்ன?**

மது அருந்துவதால் கல்லீரலில் ஏற்படும் இழைநார் வளர்ச்சி நோயின் விளைவாகத் தோன்றும் இரத்த நாள வீக்கத்தை உள்நோக்கிக் குழாய் அல்லாமல் சைல்டு புக் (Child Pugh) அளவின் மூலம் கண்டறிதல்.

**ஆய்வு முறைகள்:-**

விரிவான நோய்க்குறிப்புகளும் மருத்துவ பரிசோதனைகளும் செய்யப்படும். நோயாளிகள் அவர்கள் சம்மதத்துக்கு பின் எட்டு எம் எல் குருதி, சீரத்தில் சி.பி.சி, எல்.எப்.டி, ஆர்.எப்.டி, ஐ.என்.ஆர் உள்ளிட்ட

சோதனைகள் செய்யப்படும் அல்ட்ரா சவுண்ட் ஸ்கேன் செய்யப்படும் இரத்த நாள வீக்கம் கண்டறிய என்டாஸ்கோப்பி செய்யப்படும்.

**ஆய்வினால் மக்களுக்கு ஏற்படும் நன்மைகள்:-**

இந்த ஆய்வின் முடிவில் கிடைக்கும் தகவல்கள் சமுதாயத்திற்குப் பயனுள்ளதாகவும் எதிர்காலத்தில் நோயாளிகளுக்கு மருத்துவ தீர்வாகவும் அமையும்.

**தங்களிடமிருந்து பெறப்படும் தகவல்களின் நம்பகத்தன்மை:-**

தங்களிடமிருந்து பெறப்படும் தகவல்கள் பாதுகாக்கப்படுவதற்கான முழு உரிமையும் தங்களுக்கு உண்டு.

இந்தப்படிவத்தில் கையெழுத்திடுவதன் மூலம் தாங்கள் தங்களைப் பற்றிய விபரங்களையும், ஆய்வு நடத்தும் ஏனையோர், வரைமுறை ஒழுங்கு குழுவினர் மற்றும் சட்டத்திற்கு உட்பட்ட மருந்து கட்டுப்பாடு இயக்குநர் ஆகியோர் பார்வையிட அனுமதிக்கின்றீர்கள்.

இந்த ஆய்வில் காட்டப்படும் தகவல்கள் அறிவியல் நாளோடுகளிலோ, அறிவியல் கூட்டங்களிலோ சமர்ப்பிக்கப்படும் பட்சத்தில் தங்கள் அடையாளம் வெளிப்படுத்தப்பட மாட்டாது.

**இந்த ஆய்வில் பங்கேற்காமல் இருப்பதால் ஏற்படும் பாதிப்பு:-**

இந்த ஆய்வில் தாங்கள் பங்கேற்க விருப்பம் தெரிவிக்காத நிலையில் தங்களின் மருத்துவர் மற்றும் மருத்துவமனையில் தங்களுக்குள்ள உறவில் எந்தப் பாதிப்பும் ஏற்படாது. தாங்கள் சிறப்பாக கவனிக்கப்படுவீர்கள். மேலும் இதனால் தங்களுக்கு இழப்பு ஏதும் ஏற்படாது.

இந்த ஆய்வின் போது எனக்கு என்ன சந்தேகம் ஏற்பட்டாலும் ஆராய்ச்சியாளரை தொடர்பு கொள்ளலாம் என்பதை அறிவேன் இந்த ஒப்புதல் படிவத்தில் கையெழுத்திடுவது மூலம் இங்கு தரப்பட்டிருக்கும் அனைத்து தகவல்களும் தெளிவாக கூறப்பட்டு என்னால் முழுமையாகப் புரிந்து கொள்ளப்பட்டது என்பதை சான்றளிக்கிறேன். இந்த ஒப்புதல் படிவத்தின் நகல் என்னால் பெற்றுக் கொள்ளப்பட்டது.

பங்கேற்பவரின் கையொப்பம்:-

கட்டைவிரல் ரேகை:- இடம்:-

பங்கேற்பவரின் பெயர்:- தேதி:-

விலாசம்:-

ஆய்வாளரின் பெயர்:- இடம்:-

ஆய்வாளரின் கையொப்பம்:- தேதி:-

# ANNEXURE – V

## ETHICAL COMMITTEE APPROVAL

**INSTITUTIONAL ETHICS COMMITTEE**
**MADRAS MEDICAL COLLEGE, CHENNAI-3**

EC Reg No.ECR/270/Inst./TN/2013
Telephone No. 044 25305301
Fax : 044 25363970

**CERTIFICATE OF APPROVAL**

To
Dr.Sindhu P
Postgradaute MD(General Medicine)
Madras Medical College
Chennai 600 003

Dear Dr.Sindhu P,

The Institutional Ethics Committee has considered your request and approved your study titled **"A study on Child Pugh score as a non endoscopic predictor for esophageal varices in patients with alcoholic liver disease" No.07052015.**

The following members of Ethics Committee were present in the meeting held on 12.05.2015 conducted at Madras Medical College, Chennai-3.

| | |
|---|---|
| 1. Prof.C.Rajendran, M.D., | : Chairperson |
| 2. Prof.R.Vimala, M.D., Dean, MMC, Ch-3 | : Deputy Chairperson |
| 3. Prof.B.Kalaiselvi, M.D., Vice-Principal, MMC, Ch-3 | : Member Secretary |
| 4. Prof.B.Vasanthi, M.D., Prof. of Pharmacology, MMC | : Member |
| 5. Prof.P.Ragumani, M.S., Professor of Surgery, MMC | : Member |
| 6. Prof.Saraswathy, M.D., Director, Pathology, MMC, Ch-3 | : Member |
| 7. Prof.K.Srinivasagalu, M.D.,Director, I.I.M. MMC, Ch-3 | : Member |
| 8. Thiru S.Rameshkumar, B.Com., MBA | : Lay Person |
| 9. Thiru S.Govindasamy, B.A., B.L., | : Lawyer |
| 10. Tmt.Arnold Saulina, M.A., MSW., | : Social Scientist |

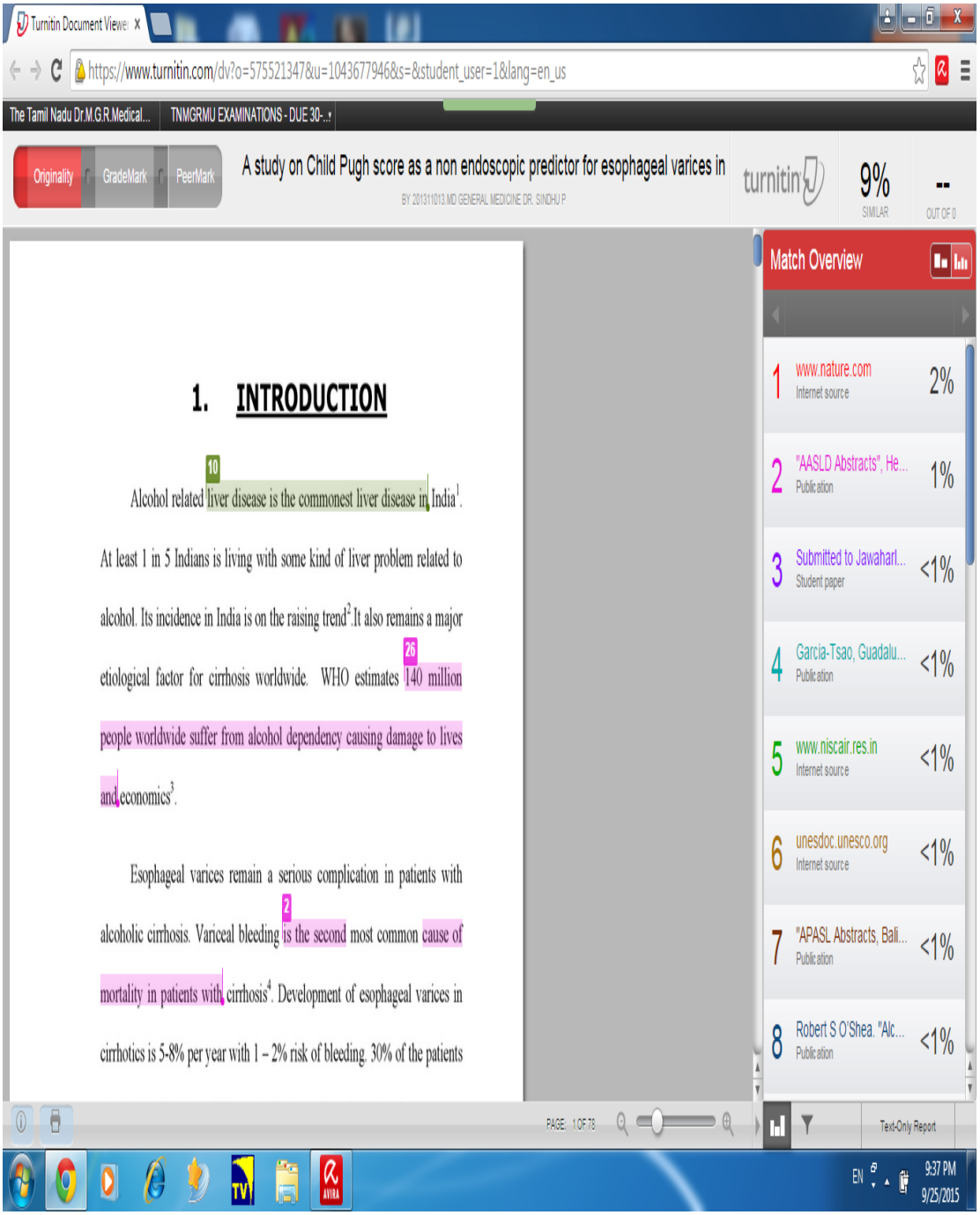
We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003

# 11. PLAGIARISM DIGITAL REPORT & RECEIPT



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| Submission title: | A study on Child Pugh score as a n.. |
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| File size: | 4.83M |
| Page count: | 78 |
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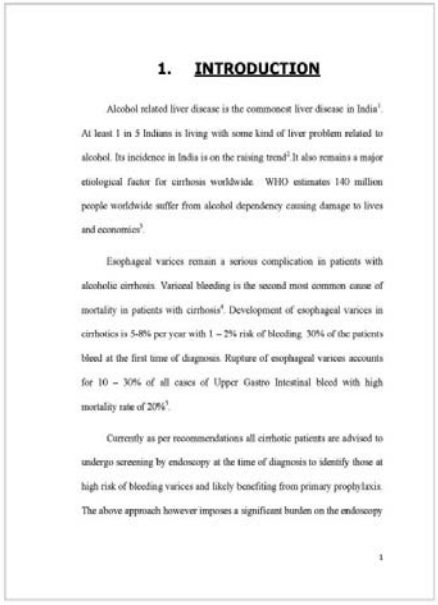
| Character count: | 40,936 |
| Submission date: | 25-Sep-2015 08:31PM |
| Submission ID: | 575521347 |



## 1. INTRODUCTION

Alcohol related liver disease is the commonest liver disease in India[1]. At least 1 in 5 Indians is living with some kind of liver problem related to alcohol. Its incidence in India is on the raising trend[2].It also remains a major etiological factor for cirrhosis worldwide. WHO estimates 140 million people worldwide suffer from alcohol dependency causing damage to lives and economies[3].

Esophageal varices remain a serious complication in patients with alcoholic cirrhosis. Variceal bleeding is the second most common cause of mortality in patients with cirrhosis[4]. Development of esophageal varices in cirrhotics is 5-8% per year with 1 – 2% risk of bleeding. 30% of the patients bleed at the first time of diagnosis. Rupture of esophageal varices accounts for 10 – 30% of all cases of Upper Gastro Intestinal bleed with high mortality rate of 20%[5].

Currently as per recommendations all cirrhotic patients are advised to undergo screening by endoscopy at the time of diagnosis to identify those at high risk of bleeding varices and likely benefiting from primary prophylaxis. The above approach however imposes a significant burden on the endoscopy

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